

The Canadian Medical Association Journal

DECEMBER 15, 1955 • VOL. 73, NO. 12

WHY DO CANCER PATIENTS DELAY?

THE GORDON RICHARDS MEMORIAL
LECTURE*

RALSTON PATERSON, C.B.E., M.C., M.D.,
F.R.C.S., F.F.R.,† Manchester, Eng.

I HAVE, for brevity, entitled this lecture "Why do cancer patients delay?" Let me amplify my intentions at once by adding the sub-title—"And what can we do about it?"

In the face of man's growing mastery of the infective and other diseases of known etiology, and of his increasing longevity, malignant disease is becoming a greater menace. The more advanced the public health services of a country, the more it becomes necessary to deploy every worthwhile weapon against cancer. If lives can be saved by successful public education towards lessening delay in seeking advice, should we be discouraged if the numbers saved thereby are not astronomical, but merely represent a modest dividend on the effort expended?

We spend substantial sums on the *treatment* of malignant disease for, at times, a very modest dividend of over-all life-saving. Look at lung cancer. Well-chosen pneumonectomy yields some 20% to 25% five-year survival of the cases operated on. Looked at against the total background of all cases occurring, there is a bare 1-2% salvage, if that. Yet a vast amount of work, both diagnostic and therapeutic, has been spread over the whole community to secure that 1-2%. It is considered fully justified in countries which have attained a high cultural level.

It, therefore, seemed to me to be important to try to determine factually the extent to which public education directed towards lessening patients' delay in seeking treatment achieves any demonstrable saving of life.

I am fully aware that astronomically large sums have been spent on just such cancer education in the United States of America and in Canada, but I am not sure whether anyone has seriously attempted to measure results objectively, or to evaluate the impact of the different methods used.

IS EARLY TREATMENT OF VALUE?

If we plan to attempt this, then clearly a preliminary question must be—"Is early treatment of proved value?" This question has also got to be brought out into the open and examined, because there are voices—and important voices at that—who make claims to the contrary. So I want first to look at the basic facts related to this question and to uncover certain common fallacies.

Much of the confusion of thought in this field, arises because of what is essentially an accepted misuse of the term "early". By dictionary definition, "early" should be used as a measure of *time*. By conventional usage in cancer work, it has been artificially applied as expressing a limited degree of advancement of disease when first seen, being early in the evolution of that patient's disease. In other words, as currently used it is a measure of *extent*, not of time.

TABLE I.

CARCINOMA OF CERVIX UTERI—CHRISTIE HOSPITAL, 1945-8 1,391 CASES FIVE-YEAR SURVIVAL RATE VS. DELAY					
Duration months.....	0-3	4-6	7-12	13-24	Over 24
% survival 5 years....	44%	39%	41%	39%	44%

If we think of it purely in terms of time, the sort of thing one can demonstrate is illustrated in Table I. The five-year survival rate is shown in relation to the stated interval between the first symptom and treatment. The results are, to all

*Presented at the B.M.A., C.M.A., O.M.A. Annual Meeting—Toronto, June 24, 1955.

†Christie Hospital, Manchester.

intents and purposes, identical for all delay intervals.

Superficial reading seems to make it quite obvious that a group of patients with, on the average, a delay of over two years before treatment did just as well as a group treated within three months, and hence that delay is, if anything, harmless. But it is utterly false to read this to mean that it is quite safe for any one individual to wait 12 or 24 months rather than three months before seeking attention. So let us be quite clear what it really does mean. It merely means that many of the patients with a long delay interval had slowly growing tumours, and so, in spite of the delay, a sufficient proportion in each delay group were still limited in extent. In that sense they were still "early". So the over-all results, group by group, were similar.

If, however, we read "early" solely in terms of its artificial meaning, as degree of advancement or clinical stage, we come back to the well-known truth that, among the treatable cancers, the patient with a growth of limited extent has a vastly higher chance of being cured. There is nothing new in the figures in Table II; they are merely shown to focus this point:

TABLE II.

COMPARATIVE SURVIVAL RATES EARLY VS. LATE			
Series	No. of cases	% well at 5 years	
		Stages I and II	Stages III and IV
<i>Cervix</i> (Heyman's 9th report)			
World Series—1947.....	6,007	51%	22%
<i>Breast</i> (Harnett 1952)			
London Hospitals Series....	2,076	46%	18%
<i>Mouth</i> —3rd statistical report, Christie Hospital Series, 1940-44.....	1,224	39%	6%

If, therefore, we succeed in bringing more cases to treatment while still in a phase of limited advancement, which in all that follows is the meaning to be applied to the term "early", more should survive.

Let us now consider what happens to any substantial block of cases of any disease, whether it be the total incidence in the community or the total intake into a hospital. If we can lessen the *average* delay interval, more cases will have come at an "earlier" stage of their disease. Note here that it becomes just as valuable to have in-

fluenced a patient who might have taken 24 months to come at 12 months, as to persuade a patient to come within three months who might have dilly-dallied for five or six months. It is the stage of advancement which matters.

The arguments based on reading "early" purely as an index of time are expounded in their simplest form by Curnow²—a misconception most beautifully argued. Russ,⁷ in an article entitled "Is early treatment essential in cancer?", propounds a somewhat similar thesis. In Canada the leading exponent of the case against early treatment seems to be McKinnon.⁴ This is not the place to discuss his various theses—each of which I believe to be false—but they may be summarized by saying that he proves early treatment to have no value. Taken to the only logical conclusion, this line of argument can only mean that treatment at any time has no value. Wisely, however, in his last paragraph he runs away from the logic of his own arguments.

There are times when statistical arguments such as these tend to confuse rather than clarify realities, so let us instead approach this question "Is early treatment of proved value?" from the simplest of angles—the individual patient. For each patient there must be a definite point in time at which the first cell which is going successfully to father a metastasis breaks loose, or when a tumour of treatable size becomes too large. If, therefore, a patient suffering from one of the more curable cancers can be persuaded to come sooner than he or she would otherwise have done, and if our medical work copes correctly, then he or she betters the probability of cure. The betterment is by an admittedly unknown amount, but it is a finite quantity! The only premise on which one could deny this would be that no treatment has ever any value.

At this point let us be clear that this does not say that cure is being promised to anyone, however early he comes, merely that his chances are improved. A very balanced assessment of this vital point was made by Kreyberg.³

"The present study seems to show that a diagnosis as early as possible is of great importance to a certain yet unknown number of individual breast cancer patients. As we do not beforehand know who will benefit and who will not, a general plea for 'early diagnosis' is fully substantiated, as every individual salvaged is important. We must, however, always have in mind that the benefit is statistically moderate and we ought to be (correspondingly) modest in our claims."

Once or twice I have used the terms "treatable cancer" or "curable cancer." Such a descrip-

tion merits a short comment in parenthesis. The surgery and radiotherapy of today *can* cure appreciable fractions of all cases occurring of some of the commoner cancers. These I call curable, for in their early stages they are as curable as many of the other less feared diseases. Patients still die from skin cancer, but far more are cured than die and show in mortality statistics as the death rate from skin cancer. Yet 100 years ago, practically all died of their disease (basal-celled growth excluded).

Other cancers can be cured in reasonable proportions of all cases treated, even if not of all cases occurring. These one may legitimately call treatable, for short. In contrast, for some cancers, such as those of the lung or of the stomach, our control is admittedly still so poor that cure must be regarded as fortuitous, rather than to be expected in an appreciable fraction. In such cancers it is not yet justifiable to attempt to persuade people to seek advice earlier than they would do in the ordinary give and take of medical practice.

WHY DO PATIENTS DELAY?

Let me turn next to a question which, in the past, has not been given as much attention as one would have expected. "What are the true reasons why patients delay?" I hope I can show you that there is more to this theme than is obvious on first glance. I should make it clear that, in all I have now to say, I am describing the contemporary English scene. Any conclusions therefrom will have to be applied with caution against the Canadian or U.S.A. backgrounds.

Some four years ago in Manchester we initiated a social survey experiment to try to find out for patients with cancers of the breast, cervix, mouth and skin the factors which really influenced the patient to seek advice. This study has been published¹ and the results have been given in detail. Here I am only concerned with broad principles.

One fact emerged early. There were two groups of patients, those who "knew", at some level of knowing, that their disease *might be* cancer, and those who "did not know". These groups are quite distinct, are mutually exclusive, and their pattern of action is quite different. Moreover, as Table III demonstrates, the two groups are distributed very differently for the different diseases.

TABLE III.

CONTRAST BETWEEN "KNEW" AND "DID NOT KNOW"
DISTRIBUTED BY DISEASE
(NUMBER INTERVIEWED: 314)

Type of cancer	"Knew"	"Did not know"	Indeterminate
Breast.....	92	31	4
Cervix.....	18	51	11
Mouth and skin.....	16	87	4

Those who do not know or suspect, inevitably can only seek advice in consonance with their ordinary approach to medicine or to doctoring. Where delay occurs it is either related to the painlessness and apparent triviality of their lesion, or to an outlook inherently antagonistic to doctoring. These quotations will illustrate:

"I suppose I'm a stupid man because I didn't worry, but I can't do with doctors and hospitals and waiting about in surgeries, so I did nothing about it."

"I never bothered because it didn't look owt, and doctors have enough to do without our keep going. Then with having it two years, I thought it were time it were mending—I'd given it a fair chance."

When they do come, the medical responsibility is the greater because of the very fact of the patient's ignorance.

In our study, as Table III shows, ignorance was the commoner state of affairs in cancer of the cervix, skin and mouth, and a minority of patients had suspicion or knowledge of the significance of the key signs.

In contrast, there is a group of patients who do know, in effect, from the beginning. They are mainly patients with cancer of the breast—92 out of 127—but when they do know, patients with cancer of the cervix or mouth act in exactly the same way. They act in one of two ways. Either they seek advice immediately—and at times suffer because their doctors are not quite so alert, or, alternatively and, sad to say more frequently, they react irrationally, almost like the rabbit hypnotized by a snake. This kind of reaction is quite clearly motivated by fear—fear of quite a deep basic compulsive origin, and by no means superficial, although camouflaged by all sorts of explanations or excuses.

One timid, elderly lady said:

"That's God's truth, and I wouldn't tell you a lie. It was just that I was frightened I'd be sent away. I couldn't help it."

A young woman laughed when she said:

"I had no time to worry about a lump in my breast. I thought of cancer, but I had a husband, two children and an ailing mother to look after, and I had four days' work a week in t'mill."

The fear results in a concealment which is curiously linked with a feeling of guilt, showing that they are aware that they ought to do something, but simply cannot bring themselves round to doing it.

The prime example of this group was cancer of the breast, in relation to the discovery of a tangible lump in the breast. One could almost say axiomatically that every adult woman knows what a *lump* in the breast *may* mean. Ignorance is rare, and the patients with breast cancer presenting in true ignorance of the significance of their symptoms tend to be those with indrawn nipple, vague general enlargement or symptoms from metastases.

There is one interesting way in which this distinction between "knew" and "did not know" actually comes out statistically. If the patient does not know, as is dominantly the case in cancer of the cervix, the time at which she will appear for advice will depend solely on the severity of the symptoms which seem to her sufficient to justify a visit to the doctor, and will have no relationship to the delay interval, since the visit depends solely on the patient's reaction to symptoms. So one would expect a similar proportion to be limited or advanced for each delay interval. This is very nearly true for cancer of the cervix, and is illustrated in Table IV, in which the patient's delay interval is contrasted with the stage of advancement.

TABLE IV.

CARCINOMA CERVIX UTERI—CHRISTIE HOSPITAL, 1950-53 1,209 CASES STAGE OF ADVANCEMENT VS. DELAY				
Duration in months.....	0-1	1-3	3-12	Over 12
% stage I and II ("early").....	59%	62%	53%	50%

In contrast, if we examine a sufficient sample of patients who deliberately delayed, we should find that the numbers with limited growths diminish as the delay interval increases. How true this is for breast cancer is shown in Table V.

The outstandingly important fact disclosed by the study was that the average delay was significantly greater with those who "know" and are motivated by fear, and was less in the face

TABLE V.

CARCINOMA BREAST—CHRISTIE HOSPITAL, 1950-53 1,194 CASES STAGE OF ADVANCEMENT VS. DELAY				
Duration months.....	0-1	1-3	3-12	Over 12
% stage I and II ("early")	74%	54%	29%	19%

of ignorance. This contrast is presented in Table VI in terms of median delay, and seems to be true equally for cancers of the breast and cervix analyzed separately.

TABLE VI.

PATIENT DELAY VS. 'KNOWING' MEDIAN DELAY IN MONTHS		
	Breast	Cervix
'Knew'.....	6	3
'Did not know'.....	2	2

If this be true, the deduction is all too clear that any education which only masters ignorance by teaching key symptoms might merely transfer a group of cases into the fear class and so augment, not lessen, the tendency to delay.

Of the two causes of delay, fear is therefore the more dominant, the more serious and the more important in causing delay. The nature of this fear therefore becomes a matter of some moment to us.

REASONS FOR FEAR

This leads me to the second study I want to consider briefly. The fear is deeply ingrained and it seemed that, to understand it, we must first find out what the ordinary person—in this particular study, the ordinary woman—thought about cancer. We therefore mounted two surveys of the Gallup Poll type to test public opinion in Manchester and Salford. One was grafted on to a study primarily directed towards tuberculosis, and in which, therefore, the cancer element was totally camouflaged. The other was a cancer study in its own right, relating to cancer of the breast and of the cervix. It was striking to find how exactly the two studies confirmed each other, even quantitatively, suggesting that their findings can be given a good measure of trust. The full details have been published,⁵ but there are certain salient findings which are pertinent to this present theme.

The most important finding was that in round figures only *one-third* of all women thought that cancer was *ever* cured. The strength of this

opinion was emphasized by comparison with a general acceptance that tuberculosis is curable, and is in contrast with a *two-thirds* figure now currently given for United States opinion surveys. It was further supported by response to the question "Have you ever heard of anyone being cured of cancer?", to which 71% answered "No".

The second point of interest concerns a lump in the breast. Out of a list of five named symptoms, no less than 40% of women chose "a painless lump in the breast" as *the most alarming*. Further questioning brought out conclusively that some 80% of all women unhesitatingly linked a lump in the breast with cancer or a tumour.

The third point is perhaps more true with us in Great Britain than with you in Canada. It is the extent to which "cancer" appears to have a sense of shame linked to it. There being of course no objective reason for this, it is to my mind psychological evidence of the innate horror with which cancer is still regarded, both consciously and subconsciously.

It is clear, therefore, that there still exists a profound ignorance in England today as to the real achievements of modern surgery and radiotherapy.

There would appear to be a more enlightened attitude in Canada. That this is so is evidenced by the findings of a similar study using identically worded questions, pioneered by the Canadian Cancer Society, to which I have been graciously given permission to refer. Quite the most impressive thing in the comparison between the Canadian survey and the Manchester one is, in fact, their almost uncanny similarity on many points. They are certainly in total agreement from all angles in recognition of the fact that a lump in the breast must be considered as potentially cancer. There is no need to teach that to anyone anywhere. There are, however, three major points on which they differ fundamentally and which are therefore of special interest:—

1. In Canada (Quebec excepted), as in the U.S.A., less than one-third of the women questioned held cancer as incurable, in contrast to the British two-thirds. Consistently with this, many more people accepted early treatment as of value.

2. In Canada, there is a greater appreciation that post-menopausal bleeding might mean cancer.

3. In Canada, heart disease is put as the second most alarming disease, not tuberculosis as in England.

It seems worth while to ask why there should be such profound ignorance of present-day realities in Great Britain. I think there are several reasons. First, it is not more than about half a century since all cancer, however simple or localized, was, in reality, almost 100% lethal. Now the race memory is long, and the processes by which its fundamental values change are slow.

Secondly, cancer, especially in Britain today, as was brought out in the survey, is a disease which still carries something of a skeleton-in-the-cupboard atmosphere. Its existence in the individual is admitted only under duress, that is to say, in the later stages. I often wonder whether we, as doctors, help to create a false public opinion in not being more outspoken. Yet to tell a patient frankly he has cancer is still contrary to majority English practice. I believe that in Canada and the U.S.A. the profession is much more frank. It is a very difficult ethical problem. It is seldom to the individual patient's own interest to know, and primarily our duty is to each patient separately. Yet there is a public health aspect to the matter. One of the consequences of this conspiracy of secrecy is that no one is ever "cured of cancer". If and when a patient dies of the disease, there is no doubt within the family as to what it was, but if he or she lives, "It cannot have been cancer after all" becomes the tacitly accepted explanation.

Lastly, let us admit as very substantial justification of public pessimism the fact that, over *all* the cancers taken together, death is still a much more common outcome than cure, and the manner of death is, by and large, often as distressing as can be.

Because of all these things, in England our primary task is still to get at inhibitions at deeper mental levels, and head public opinion in general towards a fully accepted belief that some cancers are curable, and not to think in terms of the individual potential patient. One friend of mine used to maintain stoutly that the only place to start our cancer education was with the high-school girl of from 16-20. There may be more truth than fiction to this idea, but it presupposes considerable patience. Moreover, if the idea has to be fixed into people's subconscious, as well as conscious, minds, then we must try to get it across, not only by argument but by some method

of vivid impressionist value. I confess that time was when I was somewhat anaphylactic to what we in Great Britain feel to be stunt approaches, such as Cured Cancer Clubs, public testimony from V.I.P.s and the like. I am now just beginning to wonder how the same principles could be suitably adapted to the English temperament! If what has been said be true, educational propaganda should only risk passing on to the second phase after the psychological background has been prepared, for it does seem to me to stand out a mile that it is imperative to conquer fear before we attempt to overcome ignorance by teaching early key symptoms, or we may even make things worse. Moreover, this fear reaction is too deep to be attacked directly by any kind of "don't be afraid" tactics. That gambit is, if anything, psychologically designed to accentuate a fear reaction rather than otherwise. It has all the atmosphere of advice to the swimmer hesitating on the brink of a cold pool, "Come on, don't be afraid, the water isn't really cold once you are in." It is even more disastrous to use "fear" as an instrument of propaganda. "Think what will happen to you if you don't act at once."

These, then, are some of the facts which will have to be taken into consideration when initiating new, or developing existing, schemes of public education.

There is, however, another question worth examination and that is the extent to which any scheme, be it good or bad, actually gets across to the population, so my next theme becomes "What can be achieved?"

THE MANCHESTER EXPERIMENTAL SCHEME

Anything we have done in the United Kingdom is microscopic in contrast to the American effort. Nevertheless, the last experiment I would like to describe is of interest in that some attempt was made to get objective, factual measures of the impact of the education.

The scheme was launched four years ago by the Manchester Committee on Cancer as a sharply delineated project in cancer education directed primarily towards breast and cervix cancer. A test area was selected with clearly definable boundaries and a vigorous local community life. The total population was 620,000, of which 325,000 were women. A control area of similar size and type but with no special propaganda scheme was also defined. We would

hope ultimately to be able to collect comparative figures for the two areas.

The principles followed were laid down before some of the ideas outlined above were fully crystallized, and were as follows:

First: Educational pressure was to be sustained through a continuing series of talks at small meetings. Large single "splash" efforts were, in general, avoided, and no attempt was made to secure radio or television support. The talks were, moreover, associated with an effort to maintain a constant stream of skilfully inserted paragraphs in the local papers.

Secondly: Emphasis in the talks was to be laid primarily on the curability of *some* kinds of cancer, interwoven into a substantial padding of general cancer interest. Only secondary emphasis was placed on the key symptoms of the more curable cancers. Every effort was made to avoid any of the fear-provoking slants of the "do this or else" variety.

The actual details of how the scheme was organized have been published,⁶ and in any case do not concern us here. Of one thing I am quite certain—the quality, quantity and tactfulness of the scheme could scarcely have been bettered. If, therefore, it fails in its intended object of influencing enough patients, it will fail because it is inherently wrong in concept as applied to that type of population, not because it was insufficiently applied. The whole area has been flooded with talks—and print—to saturation point, and has been kept there for some three years. In that period there have been:—

1. 400 talks at small meetings of all sorts from Rotary Clubs to Dorcas Societies, and even bowling clubs! This is an average of one every two or three days for three years in quite a limited community.

2. Over 500 paragraphs or references of some kind or other in the local press, additional to the normal quota of cancer references in the national papers.

What does concern us in this lecture is our effort to get some objective measure of the completeness of the coverage and of the effects. That study is not complete and the findings reported are still provisional. Indeed, they are to be regarded as little more than an indication of the type of thing which can be discovered. We have much more to do before the whole picture is clear.

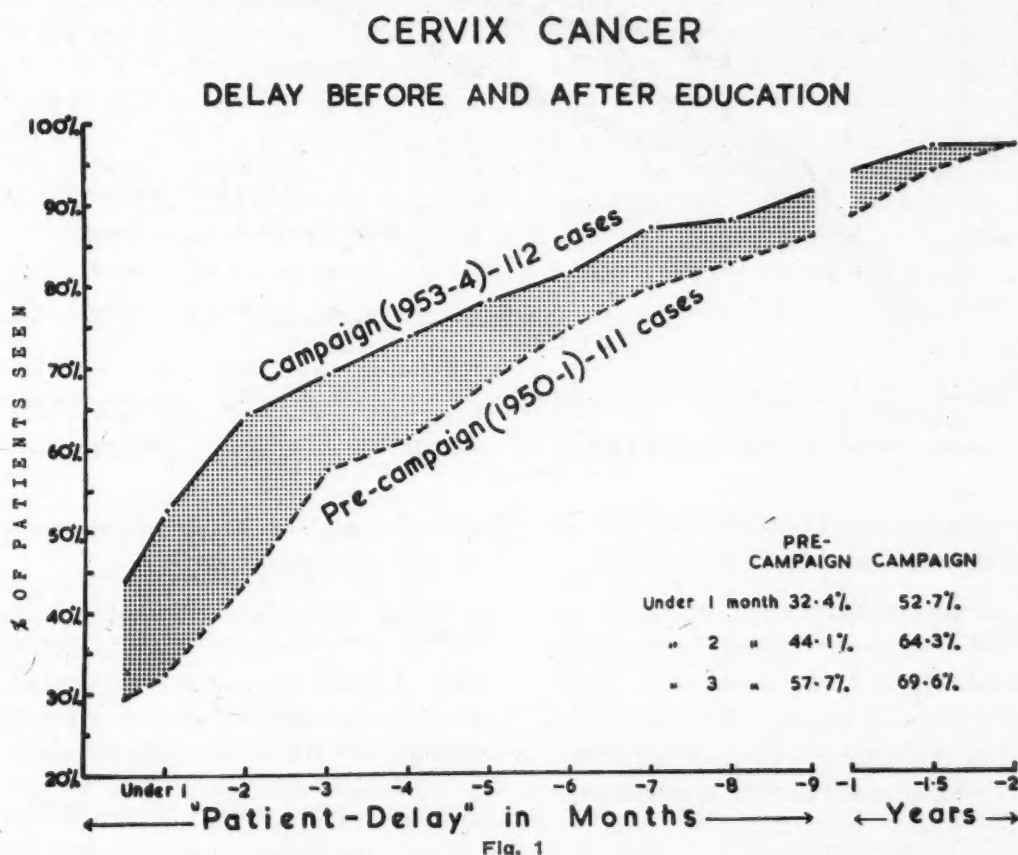
Some negative findings can safely be reported now.

1. No significant cancerophobia of any kind has been created.
2. No rush on doctors' offices has occurred.
3. No opposition was met with from the local medical profession, once the scheme was understood and seen in action.

To measure positive results is by no means as

interviews. I have not yet resolved this apparent contradiction.

In Figures 1 and 2, the shortening of the delay period is illustrated by graphing the percentage of all cases analyzed against length of delay for the pre-campaign years, 1950-51, and for the last two campaign years, 1953-54. This method of presentation has been selected, rather than average or median delay figures, as it shows that the



easy. It is being attempted in two ways. The more statistical measure is the average decrease, if any, in the delay interval between first symptom and first seeking of medical attention. This is the over-all quantitative assessment. A rather more ambitious project has also been launched—namely, to interview personally a substantial proportion of persons with newly discovered breast or cervix cancer occurring in the area in the last two years of the scheme, 1953-54, to find out what induced them to seek advice. This is, in a way, the qualitative counterpart of the other.

Strangely enough, as will be seen, cervix cancer shows a more decisive difference as measured statistically. In contrast, the impact on breast cancer cases seems more in evidence in the

betterment occurs at all intervals—and, therefore, for the slow-growing case as well as the fast.

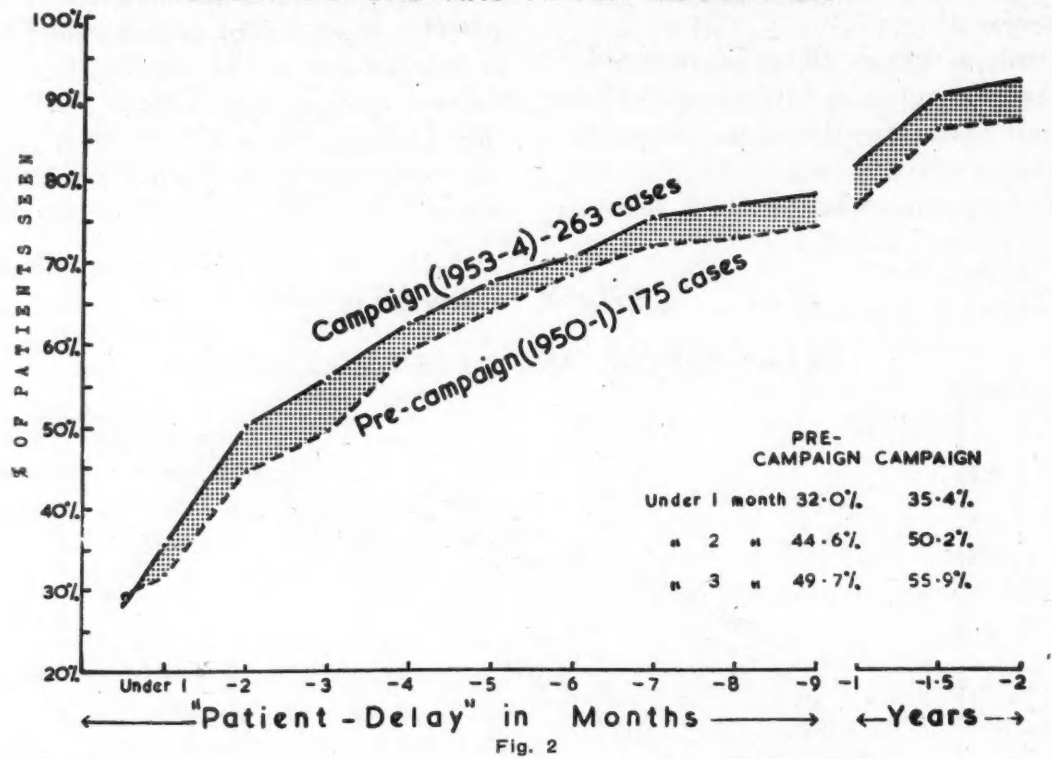
The improvement for cervix cancer would seem to be definite enough; that for breast cancer is of doubtful statistical significance.

In the interview study, the interviews were on the same lines as the delay study: they were intimate and lengthy and the patient was not directly made aware of the special purpose of the interview. In all, 320 patients were so interviewed, a stupendous undertaking.

The resultant analyses in Tables VII and VIII are to be regarded as rather more approximate, but I think they are none the less informative.

Table VII shows that for breast cancer rather more than one-third of patients proved to have

BREAST CANCER
DELAY BEFORE AND AFTER EDUCATION



been contacted at the end of a three-year period of education—a surprisingly high figure.

Of these, about one-third were influenced in the sense that they were adjudged on fairly strict criteria to have come earlier than they otherwise would have done. As will be seen, it is a good fraction of those contacted, 28 out of 86, but not a large actual number or a large fraction of the whole.

The most interesting incidental finding, not shown in the table, gave confirmation of the fear response of the previous study in 34 cases of

breast cancer. The nature of this is best illustrated by two quotations:—

"I thought the article just applied to my case, but I dismissed it and put the whole thing out of my mind."

Better still was that of the patient who, when pressed by her sister to go to a talk refused, and explained her refusal to the interviewer as

"Because I knew I ought to see to this lump."

The corresponding data for cervix cancer are in Table VIII. This, as will be seen, does not look a very promising harvest. Put from the worst angle, four cases are known to have been

TABLE VII.

BREAST CANCER—MANCHESTER STUDY IMPACT OF PROPAGANDA		
Number interviewed.....		230
In contact with propaganda:		
(a) Ours.....	52	
(b) Other.....	34	
		86
Influenced by propaganda:		
(a) Ours.....	20	
(b) Other.....	8	
		28
Influenced by relatives— stimulus unknown.....		50
Came under medical care in the usual way.....		152

TABLE VIII.

CERVIX CANCER—MANCHESTER STUDY IMPACT OF PROPAGANDA		
Number interviewed.....		90
In contact with propaganda:		
(a) Ours.....	6	
(b) Other.....	5	
		11
Influenced by propaganda:		
(a) Ours.....	2	
(b) Other.....	2	
		4
Influenced by relatives— stimulus unknown.....		13
Came under medical care in the usual way.....		73

influenced out of a total of 90. The cervix cancer study was perhaps more affected than that of breast cancer by the fact that so many patients are ignorant of the probable nature of the disease and so could not have been influenced except in terms of general hygiene.

For both series together, the numbers contacted are appreciably higher in the third year than in the second, an advance of from 22% to 36%.

The next suggestive finding concerns the effect of the two different types of propaganda. This is analyzed in Table IX, as far as these things can ever be tabulated, summing up *all* propaganda (our own special project plus that coming through the national press, etc.) as the normal undercurrent of health education, but excluding radio or television talks.

TABLE IX.

MANCHESTER CANCER STUDY, 1953-54 EFFECT OF DIFFERENT TYPES OF PROPAGANDA		
Method	Number contacted	Number influenced
Personal talks.....	11	9
Articles.....	85	23

It will be seen that, although the lectures reached far fewer people, when they did so they were much more effective, a score of 9 out of 11 influenced being almost astonishing. It must, moreover, be noted that a lot of the press material is in the form of reports of meetings.

To date, the experiment described has been confined to the mixed rural and small town experimental area. On April 1, 1955, we started a more ambitious scheme to try to study the effect of education as applied to the population of a large city area, using the Manchester conurbation as test ground. This may enable us to get some data on more massive approaches, such as radio and television.

I have told this story solely in relation to education of the public as one method of countering delay. I am fully conscious that we as a profession also carry considerable responsibility for the ultimate total delay, both at general practitioner level and at hospital admission levels. This is, however, a completely separate problem, calling equally for study and for correction. That it is not dealt with in this paper in no way implies that it is of other than vital importance.

So we come to the final question:

WHAT IS IT ALL WORTH?

Looked at from one angle, it may seem a pitifully small harvest for an effort, the intensity of which could scarcely have been augmented. Its cost was such that, applied at the same rate over the whole population of England, it would have been £125,000 (about \$345,000) per annum. At this magnitude and with these methods, it has been shown possible: (1) to contact at least one-third of the desired population successfully; (2) to prove that at least one-third of these can be influenced in some degree.

Looked at from another angle, however, it is clear that such figures may not measure the most important item of all—a gradual but very necessary alteration in public opinion in that area, which will have its effect only after a substantial latent period, and which will, I hope, parallel what you have already achieved in Canada.

Finally, let us be clear that we have as yet no data as to whether any of those patients influenced have in consequence been saved. Yet there are enough data to show that, on that critical assessment, it is obvious that public education at its best must be costly, though perhaps cumulative. So we are brought back to the unanswerable question—"What is the price of one human life?"

REFERENCES

1. AITKEN-SWAN, J. AND PATERSON, R.: *Brit. M. J.*, 1: 623, 1955.
2. CURNOW, R. N.: *Pub. Health*, 67: 112, 1954.
3. KREYBERG, L.: *Brit. J. Cancer*, 7: 157, 1953.
4. MCKINNON, N. E.: *Lancet*, 1: 251, 1954.
5. PATERSON, R. AND AITKEN-SWAN, J.: *Ibid.*, 2: 857, 1954.
6. PATERSON, R., METCALFE-BROWN, C. AND WAKEFIELD, J.: *Brit. M. J.*, 2: 1219, 1954.
7. RUSS, S.: *Ibid.*, 1: 580, 1953.

RÉSUMÉ

Le contrôle des maladies infectieuses et des autres maladies d'étiologie connue a augmenté la longévité et mis en évidence la menace de néoplasme. Si les campagnes de publicité destinées à mettre le public en garde contre le cancer coûtent très cher et sauvent peu de vies, il ne faut pas oublier que l'aspect thérapeutique du cancer est aussi fort dispendieux et guérit très peu de malades. Si l'on cherche à évaluer ce que rapportent en vies humaines les campagnes d'éducation publique dans ce sens, on doit d'abord se demander si le traitement précoce a quelque vertu particulière. Il est des tumeurs dont l'évolution est lente et pour lesquelles un retard de plusieurs mois dans l'application des traitements n'aggrave pas le pronostic. Un tel état de choses ne doit cependant pas diminuer l'importance du traitement précoce. Le problème réside dans l'étendue des lésions. Moins grande est la lésion, meilleures sont les chances de survie. L'auteur s'élève contre l'opinion de McKinnon voulant que le traitement précoce soit sans valeur. Si on considère le cas de chaque malade en particulier, il

existe certainement un moment où sa lésion jusque-là de dimensions se prêtant au traitement devient ensuite trop étendu. Sans s'engager à promettre des guérisons, l'auteur prétend tout de même que plus tôt vient un malade, meilleures sont ses chances; (il cite alors l'opinion de Kreyberg).

Le terme "guérison" n'est pas employé à la légère, puisque la chirurgie et la radiothérapie peuvent effectivement guérir un certain nombre de cas de cancer. Si la majorité des cancers de la peau peuvent être guéris, les cancers des poumons ou de l'estomac échappent encore pour le plus grand nombre à notre contrôle.

Si l'on cherche la véritable raison qui porte les malades à remettre à plus tard toute consultation médicale lorsqu'ils sont atteints de cancer, on doit faire la distinction entre ceux qui soupçonnaient fortement la présence de la maladie et ceux qui l'ignoraient complètement. Ceux du second groupe sont induits en erreur par l'apparence insignifiante de la lésion et l'absence de douleur, quelquefois secondées par une attitude de défiance à l'égard de la médecine. Si l'ignorance est surtout le fait de ceux qui sont affectés de cancers du col, de la peau et de la bouche, par contre il existe un certain nombre de malades affligés de cancer du sein qui sont au courant de leur état dès le début. Celles-ci consultent quelquefois sur-le-champ et s'irritent si leurs médecins n'agissent pas promptement, alors que d'autres, au contraire, se refusent à penser et ressemblent au lapin qu'hypnotise un serpent. La peur est évidemment à la base de cette réaction. Dans le cancer du col, l'intensité des symptômes seule porte la malade à consulter. La période de retard est en proportion des réactions de la malade aux symptômes. Les statistiques démontrent que ceux qui savent mais qui ont peur retardent plus que ceux qui ignorent.

Le résultat de deux enquêtes d'opinion publique sur le cancer du sein et du col menées séparément a montré qu'un tiers seulement des femmes interrogées, à Manchester et Salford (G.-B.), croyait qu'un cancer pût jamais être guéri—(deux tiers, en Amérique). Il fut établi par les mêmes mesures que non moins de 80% des femmes questionnées mentionnèrent le cancer comme étant la cause de bosses dans le sein. Enfin, un certain nombre de malades considèrent encore le cancer comme une maladie honteuse. En Angleterre, encore de nos jours, le cancer est un sujet tabou, au point que la majorité des médecins hésitent à en informer leurs malades. L'opinion publique peut sans doute justifier son pessimisme du fait que la mort est encore le dénouement le plus fréquent dans la majorité des cancers et que cette mort est, hélas! trop souvent, des plus pénibles.

La tâche, en Angleterre, consiste donc à diriger l'opinion publique vers l'acceptation du fait que certains cancers sont curables. Une telle entreprise a déjà été lancée par le Comité du cancer à Manchester. On procéda par une série de causeries à toutes sortes de petites réunions suivies de communiqués dans les journaux de l'endroit. On insistait surtout sur les possibilités de guérison de certains cancers, en s'abstenant bien de mentionner tout aspect pouvant provoquer la peur. L'évaluation de ces mesures est loin d'être complète; il semble cependant y avoir une diminution réelle dans le retard des cas de cancer du col à consulter. Les cancers du sein ne semblent guère avoir changés. Les causeries sont probablement le meilleur moyen de persuader le public. L'effort déployé dans cette entreprise peut paraître immense en raison du peu de résultats obtenus. En effet, un tiers seulement de la population visée fut atteint et, seul, un tiers de celui-ci put être influencé de quelque manière.

M.R.D.

INDICATIONS FOR AND RESULTS OF SURGERY FOR MITRAL STENOSIS*

PAUL DAVID, M.D.,† *Montreal*

WE BECAME INTERESTED in the surgical treatment of mitral stenosis in February 1950 when Dr. Edward Gagnon performed on one of our patients his first mitral commissurotomy. Up to December 31, 1954, 100 patients were treated surgically and followed up by us at Notre Dame Hospital, Montreal. We then took charge of the Montreal Institute of Cardiology where a further 84 patients were operated upon up to June 1, 1955. The medical care of these patients was the responsibility of one of the Institute cardiologists and operations were performed by Dr. Edward Gagnon or Dr. Arthur Vineberg.

We will not try to summarize the large number of articles written on mitral stenosis in the

last five years. We prefer to give the personal thinking of our group and the results of our clinical studies.

1. MEDICAL EVOLUTION OF MITRAL STENOSIS

It is important to accumulate data on the clinical course in cases of mitral stenosis.*In collaboration with Dr. Yves Desrochers, the cardiac anatomy of patients dying of mitral stenosis in Notre Dame Hospital from 1945 to 1953 inclusive has been reviewed (Table I). This study

TABLE I.

N.D.H. MEDICAL DEATHS DUE TO MITRAL STENOSIS (1945-1953)

	No. cases	Average age at death
Male.....	21	42
Female.....	34	44
Total and average age....	55	43

DEGREE OF NARROWING AND AVERAGE AGE AT DEATH

Mitral valve circum.	— 4.5 cm.	+ 4.5 cm.
No. cases.....	27	28
Age at death.....	35	49

*Presented at the Conjoint Meeting of the British, Canadian and Ontario Medical Associations, Toronto, June 20, 1955.

This work was supported by a grant from the Department of National Health and Welfare of Canada.

†Director of the Montreal Institute of Cardiology.

was limited to non-surgical cases. Of 55 patients 21 were male and 34 female. The average age at death in this total group was 43 years. The tip of the index finger has an average circumference of 4.5 cm. and we considered as "tight" mitral stenosis a mitral valve in which the circumference was 4.5 cm. or less. In the group studied, the stenosis in 27 cases was "tight" by these standards and the average age at death for this group was 35. In the cases with mitral stenosis above this limit, the average age at death was 49. From this study it seems reasonable to conclude that the life span in mitral stenosis is markedly related to the degree of narrowing of the valve. It seems that the evident discrepancies in the medical literature on the average span of life in mitral stenosis are possibly due to the fact that the degree of narrowing was not sufficiently taken into account. Most articles were written before the advent of cardiac surgery, and for this reason the importance of this factor may have been overlooked.

In our series of 184 patients, 132 were females and 52 were males. The average age at the time of operation was 33. With very few exceptions, all these patients had a tight mitral stenosis. It is of interest to realize that our patients sought the help of surgery two years before their estimated age of death.

We invite other workers to repeat this study with a view to determining the influence of the degree of narrowing on the average span of life. This study gives a clue, but no more, because the number of cases is too small.

2. WHAT ARE THE INDICATIONS AND CONTRAINDICATIONS IN MITRAL COMMISSUROTOMY?

It would be simple, pleasant and practical to evaluate a candidate on rigid criteria and base the decision for operation on a mathematical summation of findings. We have tried to do so within certain limits. With increasing experience we feel more and more certain about factors for or against an operation. At the same time we realize that many problems are not yet settled and that every candidate is a problem *per se*. It must be remembered that mitral commissurotomy does not pretend to cure the patient, because mitral stenosis is only the end result of a rheumatic heart disease in which the surgeon restores to normal the hæmodynamics in the lung area and left side of the heart. It even seems

sufficiently proved that, in a certain number of patients, the operation provokes a flare-up of rheumatic activity.

The main indication for commissurotomy is to rehabilitate the patient with a tight mitral stenosis by giving him a more agreeable life and happiness. If for physical, social or psychological reasons this end result cannot be achieved, the operation, even in presence of good surgical risk, should not be considered.

Let us now try to analyze the factors affecting evaluation of a patient. These factors are divided into three groups: for operation, questionable, and against operation (Table II).

For operation:

Symptoms.—Every doctor is familiar with the usual symptoms, chronic or acute, of mitral stenosis: shortness of breath on exercise, hæmoptysis, pulmonary œdema, pulmonary or peripheral embolization, physical disability and fatigue.

Signs.—We like to operate on a patient who is under 45 and has typical auscultatory signs of pure mitral stenosis.

ECG—The electrocardiographic findings compatible with mitral stenosis may be the following: normal tracing, sinus rhythm, an electrical axis of $+75$ or more, left auricular hypertrophy, right ventricular hypertrophy with or without strain, minor right auricular hypertrophy and fibrillation with well-controlled ventricular rate.

X-ray.—By x-ray, the size of the heart should be normal or slightly enlarged. There should be a mitral configuration with or without pin-point calcification.

Laboratory.—Negative tests for rheumatic activity, antistreptolysin, CRPA, normal sedimentation rate, a normal venous pressure and normal kidney function are essential.

Catheterization.—Except for research purposes, there is no indication for catheterization in this category of patients.

Against operation:

A candidate should not systematically be turned down because of the presence of one of the negative factors to be enumerated. But the presence of any of these factors compromises the long-term result of commissurotomy, and for this reason such a patient should always be very carefully assessed before surgery is recommended.

TABLE II.

INDICATIONS FOR AND CONTRAINDICATIONS TO COMMISSUROTOMY			
	<i>For</i>	<i>Questionable</i>	<i>Against</i>
<i>Symptoms</i>	Shortness of breath. Hæmoptysis. Acute pulmonary oedema. Embolus. Physical disability. Fatigue.	Pregnancy.	Orthopnoea resistant to usual treatment. Mental disturbances.
<i>Signs</i>	Under 45 years Mitral stenosis with typical auscultation.	45 to 55. Systolic xiphoid, precordial or apical murmur not radiating to axilla. Slight aortic stenosis or regurgitation. Diastolic murmur left border of sternum with normal blood pressure. Well-controlled right heart failure.	Over 55. Presence of mitral regurgitation. Marked aortic valvular disease. Uncontrollable right heart failure.
<i>ECG</i>	Normal. + 75 and more axis. Right ventricular hypertrophy. Left auricular hypertrophy. Minor right auricular hypertrophy. Well-controlled auricular fibrillation.	+ 30 to + 75 axis. Uncontrollable auricular fibrillation.	Less than + 30 axis. Left ventricular hypertrophy.
<i>X-ray</i>	Normal size or slightly enlarged heart. Mitral shape. Pin-point calcifications.	Possible left ventricular enlargement.	Markedly enlarged heart. Left ventricular enlargement. Gross calcification.
<i>Laboratory</i>	Negative tests for rheumatic activity. Normal venous pressure. Normal renal function.	Doubtful signs of rheumatic activity.	Positive tests for rheumatic activity. + 200 and more venous pressure. Abnormal renal function.
<i>Catheterization</i>	Not indicated.	Indicated.	Not indicated.

Symptoms.—Persistence of orthopnoea or hæmoptysis in a well-treated patient is often a sign of irreversible pulmonary vascular anatomical damage that may not respond to surgery. This seems to be true except in pregnancy. Mental disturbances such as marked imbalance, neurosis or psychosis remain and often are aggravated by the surgical procedure. These patients very often remain incapacitated even when the organic symptoms are obviously alleviated.

Signs.—After 55, in the majority of cases, irreversible aging changes occur. Nevertheless if this is the only single factor against the operation, we would certainly operate.

Surgery is not recommended in the presence of a fair amount of mitral regurgitation, of moderate aortic insufficiency, and of uncontrollable right heart failure.

ECG.—Operations on patients with an electrical axis less than +30 or with a tracing showing left ventricular hypertrophy have often given poor results.

X-ray.—Surgery must be avoided when the heart is markedly enlarged, in the presence of gross mitral calcification or marked left ventricular enlargement. There is a real radiological difficulty in evaluating right and left ventricular hypertrophy. I personally feel that the electrocardiogram is much more reliable for this estimation than the x-ray picture.

Laboratory.—Operation should not be done with positive tests for rheumatic activity, when the venous pressure is elevated above 200 mm. of water, and when kidney function is poor.

Catheterization.—In this group of patients, heart catheterization is rarely indicated because many negative factors are usually present in the same individual.

Questionable factors:

Symptoms.—We have had the opportunity of seeing some cases of mitral stenosis associated with pregnancy. The findings in these cases have been summarized by our associate, Dr. Leon Lebel, and will be published shortly. Surgery is indicated when the symptoms, as seems usual, are not improved by medical treatment, especially hæmoptysis and subacute pulmonary œdema. We were fortunate, in seven such candidates, in having no maternal mortality and only one abortion.

Signs.—Between the ages of 45 and 55, operation should be considered if the other factors are favourable.

Operation can be performed with some degree of aortic insufficiency, when the regurgitation is not reflected by the blood pressure. Of course, in the presence of a diastolic murmur along the left border of the sternum we face the problem of a possible Graham-Steel murmur. Heart catheterization is recommended when evaluation of this murmur is not possible by the over-all picture. We discuss the opportunity of commissurotomy in the presence of well-controlled right heart failure. In this group the results have been variable. The assessment of this factor depends more on the addition of negative and questionable signs than on the right heart failure itself. The problem of interpretation of a systolic apical murmur will be discussed later. This is probably the most difficult factor to assess in the evaluation of mitral stenosis.

X-rays.—As already mentioned, the most questionable radiological factor is the proper interpretation of enlargement of right and left ventricles.

Laboratory.—In cases with doubtful signs of rheumatic activity, operation should be postponed. By repeating the tests and re-examining the patient from time to time, some definite decision can eventually be reached.

Catheterization.—It is usually in cases with these questionable signs that catheterization of the right cavities and of the pulmonary artery is important. This procedure has a definite value in the diagnosis of tricuspid valvular disease and in the evaluation of a diastolic murmur along the left border of the sternum.

In our opinion, prophylactic operation should not be performed and we are more and more convinced that so-called "salvage operations" most often give poor results.

3. EVALUATION OF THE SYSTOLIC MURMUR

As already mentioned, the proper evaluation of a systolic murmur anywhere between the xiphoid area and the left axilla is often difficult. In trying to find some clues to this problem a review of the first 150 consecutive surgical cases was done with Dr. O. Gialloredo of the Institute and will be published shortly. Some of the most significant findings are summarized in Table III.

TABLE III.

SYSTOLIC MURMUR IN MITRAL STENOSIS (First 150 consecutive commissurotomies)		
Maximum of auscultation	Number	%
Cases.....	73	48.6
Apex.....	39	53.0
Precordium.....	10	14.0
Xiphoid.....	24	33.0
Irradiation to axilla		Number
Cases.....		20
Regurgitation.....		16
Regurgitation		
Cases.....		19
Minimal.....		13
Fair.....		4
Marked.....		2
Tricuspid insufficiency		
Proved.....		12
Probable.....		15
Summary		
Mitral regurgitation.....		19
Proved T.I.....		12
Probable T.I.....		15
Total.....		46
Unknown.....		27

Seventy-three patients (48.6%) in this series had, prior to operation, a systolic murmur at the apex, the xiphoid area or somewhere in between. It seems significant that of 20 cases where the murmur was heard in the left axilla, 16 had regurgitation as judged by the surgeon's finger. This leaves only three patients with regurgitation and no murmur in the axilla. Definitive proof of tricuspid insufficiency based on clinical and catheterization studies was found in 12 patients and probable tricuspid incompetence, based on clinical grounds alone, in 15. With these figures in mind the systolic murmur is explained in 46 patients, leaving 27 with a murmur, in whom the surgeon did not find regurgitation and in whom no evidence of tricuspid regurgitation could be found. The problem of the systolic murmur remains a field of fascinating clinical investigation. It is felt that it does not, in many instances, represent organic mitral regurgitation.

Tricuspid valve disease, either organic or functional, is probably a neglected entity today and will be more and more recognized in the future.

4. COEFFICIENT CHART

After reviewing the mortality and the results of the first 75 consecutive operations we found that our conception of evaluating the operative risk and the results was not very satisfactory because it was mainly based on the patients' subjective symptoms. We all know that some patients have advanced heart disease with few symptoms and vice versa. It was soon realized that in the years following operation some patients had few objective changes and yet felt greatly improved. It was believed that a summation of the subjective and the objective findings might give a better evaluation of suitability for surgery. By assigning a coefficient to each sign, tables were drawn up and our patients divided into four groups. It is not suggested that this table is 100% correct. With more experience, it may be found that certain factors were underestimated or overestimated or even overlooked. Such a coefficient chart is shown in Table IV. A more standard classification of the

TABLE IV.

PREOPERATIVE EVALUATION OF PATIENT	
Findings	Coefficients
Age (+ 45).....	2
Dyspnoea.....	1 or 2
Orthopnoea.....	2
Pulmonary oedema.....	1
Hæmoptysis.....	1
Embolus.....	1 for each episode
Right ventricular failure.....	3
Mitral regurgitation.....	2
Aortic stenosis.....	2
Aortic insufficiency.....	2
Tricuspid insufficiency.....	1
X-ray enlargement.....	1 to 3
Chronic pulmonary disease.....	1
Calcification.....	2
Fibrillation.....	2
Paroxysmal arrhythmia.....	2
ECG right ventricular hypertrophy.....	1 or 2
Group	
I.....	1 to 5
II.....	6 to 10
III.....	11 to 15
IV.....	16 and +

same patients based on their physical ability to work was also made:

Grade I = no disability; Grade II = slight disability; Grade III = moderate disability; Grade IV = marked physical disability.

Unfortunately the use of the coefficient chart is restricted in the postoperative patients. Murmurs, electrocardiographic changes, and the x-ray picture are unreliable postoperatively, as they are infrequently altered by surgery. However, the coefficient method of grouping patients before operation gives a much more exact picture of the disease than one based on factors of disability alone.

For example, one patient had not worked for two years because of hæmoptysis. He had a total disability. Nevertheless he was in our Group II. Another patient had only paroxysmal attacks of tachycardia and in between could carry on an active life. She was fibrillating and had a calcified valve, marked radiological enlargement, right ventricular hypertrophy electrocardiographically with strain and some questionable aortic regurgitation. She was therefore in Group I based on physical disability and in Group III in our coefficient chart.

5. OPERATIVE FINDINGS

Applying these criteria, 184 patients were submitted to surgery up to June 1, 1955. The findings of the surgeons are summarized in Table V. In every case except two there was a

TABLE V.

OPERATIVE FINDINGS IN FIRST 184 CONSECUTIVE CASES	
No. of cases	Operative findings
182	Mitral stenosis
	163 No regurgitation
	13 Minimal regurgitation
	4 Fair regurgitation
	2 Marked regurgitation
1	Mitral insufficiency
1	No mitral valvular disease

tight mitral stenosis, and a commissurotomy was performed. The diagnostic percentage of error is thus 1.09%. This is sufficiently low to deter us from starting more complicated techniques in evaluating the degree of possible regurgitation such as electrokymography, direct or bronchial needling of the left atrium for pressure recordings, or angiocardiology. In the remaining 182 patients, with a tight mitral stenosis, two had marked (1.08%), 4 fair (2.17%), and 13 minimal (7.06%) regurgitation.

6. OPERATIVE MORTALITY AND LATE DEATHS

Let us consider very briefly the mortality in our series. In Table VI the surgical mortality

TABLE VI.

Years	MORTALITY		
	No. cases +	No. deaths	%
1950.....	5	2	40.0
1951.....	19	3	15.8
1952*.....	35	6	17.1
1953.....	41	4	9.8
1954.....	55	3	5.5
1955-June 1.....	27	2	7.4
Total.....	182	20	10.9

*Two late deaths:
20 months (sudden).
15 months (automobile accident).
+Two cases of diagnostic error not included.

by year has been reviewed. The two cases of diagnostic error are excluded. It is clear that the risk has decreased with the increasing experience of the surgical as well as the medical group.

work was done by Drs. Pierre and Gilles Legault of our staff.

Twenty-eight cases were not included: there were 18 postoperative deaths, the preoperative record of one was inadequate, and 9 cases could not be traced for this study.

This leaves 89 cases reviewed in the last three months: 76 patients have been re-examined by our group and 13 evaluated indirectly by contact with their doctor, our social service or personal letters.

All our findings are summarized in Fig. 1. It illustrates the discrepancies already referred to between the standard and the coefficient chart in evaluating the patient preoperatively.

When judged by their physical disability, the number of patients in each group is the following before the operation:

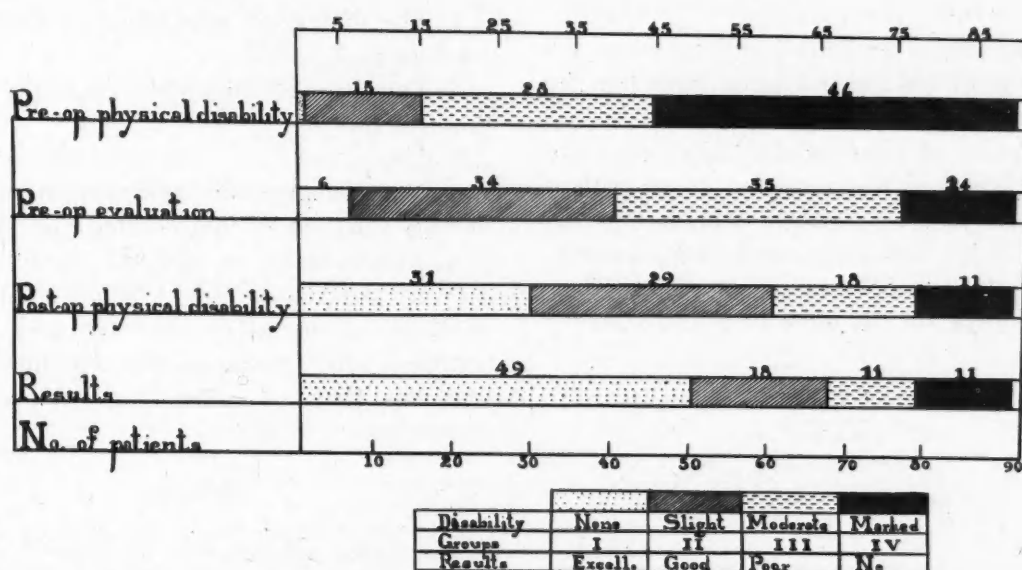


Fig. 1

From a peak of 40% in 1950, operative mortality fell to a minimum of 5.5% in 1954, the average being 10.9%. There have been two late deaths since; one patient died suddenly in Florida 20 months postoperatively and no autopsy was performed. The other died a few minutes after an automobile accident.

7. RESULTS

The assessment of results of commissurotomy has been limited in this study to patients followed up for more than 12 months. The first 117 cases have therefore been reviewed with a follow-up ranging from 12 to 64 months. The statistical

Group I = none
Group II = slight = 15 patients
Group III = moderate = 28 patients
Group IV = marked = 46 patients

With the coefficient chart the same patients were distributed as follows:

Group I = 6 patients
Group II = 34 patients
Group III = 35 patients
Group IV = 14 patients

The postoperative results were estimated first in terms of subjective appreciation by the patient of his disability. This evaluation gives the following:

Group I = no physical disability	= 31	} 67.4%
Group II = slight	= 29	
Group III = moderate	= 18	} 32.6%
Group IV = marked	= 11	

Secondly came objective evaluation of the examiner who, by comparing the preoperative and postoperative findings, estimated the result of surgery as excellent, good, poor or nil. This evaluation takes into account the clinical findings, the x-ray picture, the electrocardiogram and the circulation time. This evaluation gives:

Group I = excellent	= 49	} 75.2%
Group II = good	= 18	
Group III = poor	= 11	} 24.8%
Group IV = no improvement	= 11	

This postoperative evaluation of the series shows from 67.4%-75.2% satisfactory results and from 32.6%-24.8% unsatisfactory results, depending on the method of evaluation.

It would seem preferable to evaluate the candidate both before and after operation by the over-all clinical picture rather than by the single criterion of physical disability. We have personally assessed the result in every patient of this study and we strongly suggest that the figures of 75.2% satisfactory and 24.8% unsatisfactory results represent the exact picture (Fig. 2). Nevertheless, for the more sceptical elements

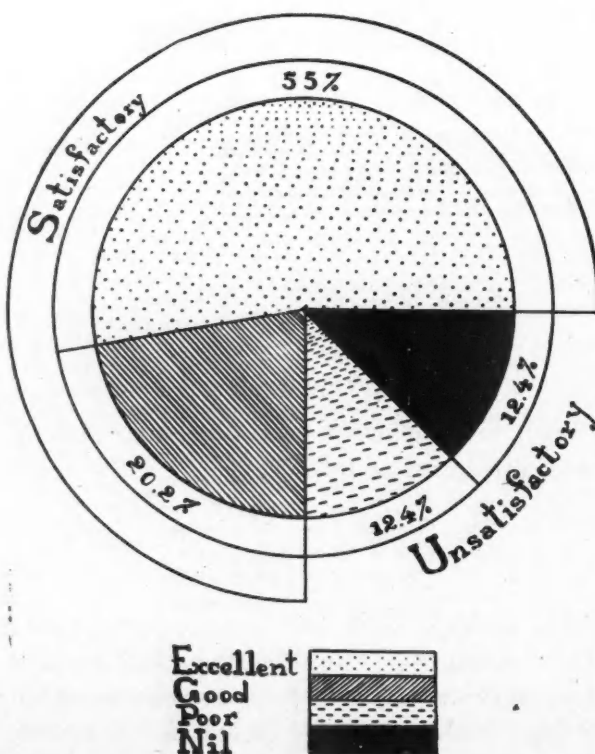


Fig. 2.—Results.

it is felt that the 67.4% satisfactory and 32.6% unsatisfactory results still represent a situation which speaks in favour of the operation.

CONCLUSION

1. The life span in mitral stenosis without operation seems to be proportional to the degree of narrowing of the valve. The average age at death in tight mitral stenosis, namely of 4.5 cm. or less circumference, is 35. The average age of 184 patients operated upon in our series is 33. It thus appears that patients require the help of surgery approximately two years before the estimated age of death.

2. The indications for and contraindications to mitral commissurotomy have been discussed, by analyzing factors which are in favour of or against operation, or are questionable.

3. A coefficient chart has been presented for the preoperative evaluation of patients.

4. The diagnostic percentage of error in this total group is 1.09%.

5. The over-all operative mortality in this group is 10.9%.

6. The results of commissurotomy on 89 surviving patients with a follow-up from 12 to 64 months vary, depending on the type of evaluation. When based on physical disability alone they are satisfactory in 67.4% and unsatisfactory in 32.6%. If based on the summation of preoperative and postoperative findings by the examiner they are satisfactory in 75.2% and unsatisfactory in 24.8%.

RÉSUMÉ

1. La durée de vie d'un malade souffrant de sténose mitrale semble proportionnelle au degré du rétrécissement de l'appareil valvulaire. La durée moyenne de vie d'une sténose mitrale serrée, c'est-à-dire, dont la circonférence est inférieure à 4.5 cm, est de 35 ans. L'âge moyen des 184 patients de cette étude est de 33 ans. Les malades semblent donc demander le secours chirurgical deux ans avant l'âge moyen de leur mort.

2. Les indications et contre-indications à la chirurgie mitrale ont été discutées en analysant les facteurs qui sont discutables et ceux qui sont en faveur ou contre l'opération.

3. Une charte de coefficients a été présentée pour l'évaluation préopératoire des malades.

4. Le pourcentage d'erreur de diagnostic de notre série est de 1.09%.

5. La mortalité opératoire de tous les malades de cette série est de 10.9%.

6. Les résultats de la commissurotomie étudiés chez 89 malades qui ont un recul de 12 à 64 mois, varient selon les critères d'évaluation. Lorsque les résultats sont basés sur l'invalidité seulement, ils sont satisfaisants dans 67.4% des cas et non satisfaisants dans 32.6%. Lorsqu'ils sont évalués par l'examineur qui essaie de tenir compte de tous les facteurs, les résultats sont satisfaisants dans 75.2% des cas et non satisfaisants dans 24.8%.

P.D.

BERNHEIM'S SYNDROME
 TERMINATING IN NEPHROSIS*

J. D. GRAY, M.D.† and
 S. T. LAUFER, M.D., F.A.C.P.,‡ Halifax

OCCASIONALLY there occurs in the progression of a fatal illness a complication which, although logically arising from the primary process, may illuminate in a tangential manner the cause of the disease not normally related. The following patient had an aortic stenosis when first seen, and 10 years later died with a nephrosis not unconnected with the condition of his aortic valves.

HISTORY

A white male, aged 18, was first seen in March 1944 with complaints of palpitation. He did not admit shortness of breath. The pulse rate was 72, there was no dependent oedema, the liver was not enlarged and the lung bases were clear. He had the typical thrill of an aortic stenosis, and a loud systolic murmur, followed by a well-marked aortic second sound. There was left ventricular hypertrophy. The phonocardiogram showed a typical diamond-shaped murmur. Vital capacity 3,300 c.c.

TABLE I.

BLOOD CHEMISTRY FINDINGS DURING THE NEPHROTIC PERIOD							
Date	Plasma protein g. %	Non-protein nitrogen mg. %	Urea mg %	Potassium mEq. /l.	Sodium mEq. /l.	Chlorides mEq. /l.	Cholesterol mg. %
August 1953.....	4.5	—	—	—	—	—	—
January 1954.....	3.0	—	20	4.7	142	106	518
June 1954.....	5.2	50	44	5.3	146	104	—
August 1954.....	4.5	26	—	4.9	152	105	253
September 1954....	4.9	77	85	4.2	146	—	—
November 1954....	—	126	146	—	—	—	—

In May 1944, a diastolic murmur was audible for the first time; it was of a blowing character; later as the disease progressed, it became rougher and rougher. In October 1945, the patient was still working. He now complained of occasional bouts of shortness of breath, the B.P. was 124/50 mm. Hg, the systolic murmur over the aortic area was rougher, the second aortic sound was still audible. By June 1946, the systolic murmur and thrill were more marked; the aortic second sound could no longer be heard. The B.P. was 130/40. In August 1947, the first signs of cardiac failure appeared. The electrocardiogram showed an inversion of T wave in Lead I and point V5 and V6. The B.P. was 130/30.

In 1950 he began having attacks of anginal pain. The heart by now was markedly enlarged; the murmur over the aortic area was to and fro. X-ray examination showed marked enlargement of the heart to the left with prominence of the first part of the aorta, seen best in the left anterior oblique position. In October 1952 the B.P. was 170/90 and remained elevated until January 1953, when it again fell to 126/30 and 120/0. In July 1953,

*From the Pathological and Cardiological Departments of the Halifax Infirmary, Halifax, Nova Scotia.
 †Pathologist.
 ‡Cardiologist

oedema of the lower limbs first appeared. It did not appear related to cardiac failure, but with intensive restriction of salt it disappeared, only to reappear a month later and remain until his death. There was no evidence of pulmonary congestion. His urine showed marked albuminuria, his liver was slightly enlarged. The urinary output of albumin was 7.9 g. per 24 hours at rest and 20 g. per 24 hours while up and about. His serum protein level was 4.5 g. A diagnosis of superadded nephrosis seemed reasonable.

By January 1954 the B.P. was 112/0, liver was not enlarged, oedema of the legs and the aortic murmurs were very marked. A chest radiograph confirmed the grossly enlarged heart, absence of pulmonary congestion and calcification in the region of the aortic valve. Venous pressure was 65 mm. Circulation time 17 seconds. Vital capacity of the lung 3,200 c.c. The electrocardiogram was consistent with hypertrophy of the left ventricle and intraventricular block.

In August 1954 he had a thrombophlebitis in the left leg which eventually subsided. The oedema was more generalized; free fluid in the abdomen was noted. By November 1954 it was evident that the disease had nearly run its course, and he died early in that month. Throughout his illness, he was treated symptomatically. Blood chemistry findings are shown in Table I.

Table II shows the findings in fluid drained from the legs by Southey's tubes.

AUTOPSY FINDINGS

Autopsy was restricted by the relatives to a six-inch abdominal incision, but the parts of interest were fairly easily obtained in spite of this imposition. The lungs

TABLE II.

ANALYSIS OF THE (EDEMA FLUID (July 1954)	
Sodium.....	152 mEq./l.
Potassium.....	4 mEq./l.
Chlorides.....	107 mEq./l.
Protein.....	Less than 10 mg. %

felt dry; the left lower lobe was removed for further examination, but section showed no gross abnormalities. The weight of the heart was 715 g. The left ventricular muscle was enormously hypertrophied, the wall measuring 4 cm. in thickness. The left auricle appeared normal. The mitral valve was free of disease and admitted the tips of two fingers only. From the root of the aorta to the cusps of its valves spread a rigid calcified circular plaque embracing all the contained structures. Between the rigid cusps was a linear opening 1.5-2 mm. in diameter, the only communication between the ventricle and aorta. On the apposite surfaces of the cusps were many calcified verrucae. The right and left cusps presented as a single cusp with a thin ridge between, suggesting an ill-formed single valve; the posterior cusp

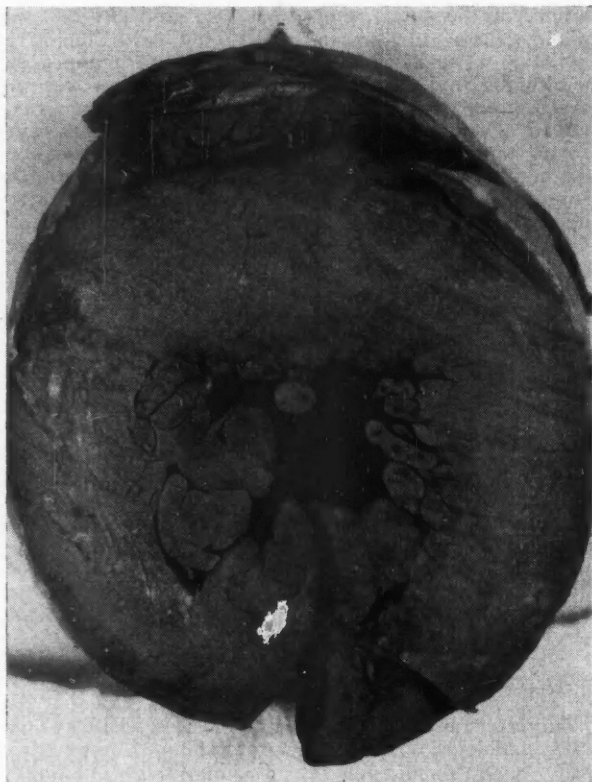


Fig. 1.—Heart in cross section, showing the gross hypertrophy and bulging of the interventricular septum with stenosis of the right ventricle.



Fig. 2.—Right ventricle opened to show the medial cusp of the tricuspid valve pushed outward by the interventricular bulge.

was a distinct entity; the picture suggested a bicuspid aortic valve, probably a congenital anomaly. The mouths of the coronary arteries were not calcified and the arteries themselves were normal. The intima of the aorta was bile-stained.

On opening the right ventricle, we noted that the interventricular septum had so hypertrophied as to bulge and nearly fill the cavity of the ventricle. The pulmonary valve was normal. The tricuspid valve was apparently normal, but on passing the hand from the right auricle to the ventricle, with the parts in their normal anatomical relationship, we found that the medial cusp of the valve had been so pushed over by the interventricular septal mass as to flatten the anterior and posterior cusps against the right ventricular wall, thus forming a functional tricuspid stenosis. The right ventricle wall was 6 mm. thick. The right auricle itself was enormously dilated, the wall being 1 mm. thick.

The liver was small and the cut surface showed obliteration of the normal architectural pattern. The kidneys were of normal shape, the capsule stripped readily, and the respective weights of the organs were 250 and 255 g. The cut surface showed the usual cortico-medullary pattern. Fig. 1 shows the heart in cross section, Fig. 2 the bulging of the interventricular septum into the right ventricle.

HISTOLOGY

Sections of the lung tissue showed no change from the normal. The alveoli were noticeably free of exudate and the pulmonary arteries showed no evidence of hypertension.

The heart muscle contained patchy areas of ischaemic necrosis at various stages of intensity; in some there was nothing but pale ghost-like areas of muscle with marked peripheral capillary congestion and histiocytic proliferation, in others of recent origin the muscle fibres had lost their ability to take up eosin. There was no evidence of sclerosis in the vessels examined, suggesting that the anoxaemia responsible for the necrosis arose from an inability of the vascular tree to keep pace with the gross hypertrophy of the myocardium. In the liver there was extreme chronic venous congestion, which had gone on to ischaemic necrosis over large parts of the parenchyma (Fig. 3).

The kidneys showed moderate cloudy swelling of the tubules and interstitial oedema only. The glomeruli were within normal limits, the common histological finding

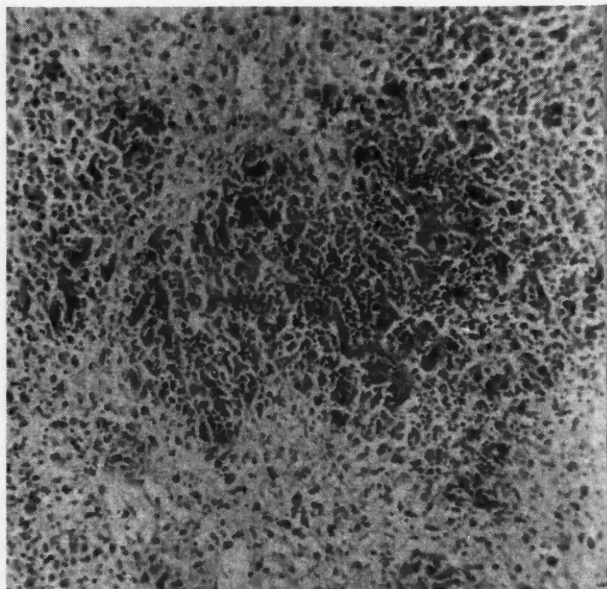


Fig. 3.—Extreme venous passive congestion of the liver which has led to ischaemic necrosis. $\times 80$.

in nephrosis. However, the renal veins presented a most remarkable picture; the right was nearly occluded by a laminated thrombus firmly adherent to the vessel wall, from which there was evidence of beginning organization (Fig. 4). In the left, an old recanalized thrombus was seen. To this had been added a more recent clot that not only nearly blocked the main lumen but also one of the reopened canals (Fig. 5). Thus from anatomical considerations the chain of events appeared to be, first, a congenital bicuspid aortic valve undergoing calcification and partial stenosis, which led to an enormous hypertrophy of the muscle of the left ventricle; that in turn almost occluded the right ventricle, leading to extreme venous stasis and, due to the last, bilateral thromboses of the renal veins, which precipitated the nephrosis. The immediate cause of death was hepatic damage and extrarenal uræmia.



Fig. 4.—Right renal vein showing laminated thrombus adherent to the vessel wall. $\times 40$.

DISCUSSION

The paradox of left heart disease with right heart failure was first described by Bernheim in 1910. Mazzei,⁸ Russek and Zohman,^{9, 10} and East and Bain⁴ have added to an understanding of it. Agreement appears to be general that the progress of the disease can be divided into stages: first, interference with filling of the right ventricle by the hypertrophy and bulging of the interventricular septum is compensated by dilatation of the right ventricular infundibulum and enlargement of the right auricle; when this

compensatory mechanism fails, the second stage sets in, characterized by systemic venous engorgement without disturbance of the pulmonary flow. The final stage is indicated by total cardiac failure and concomitant embarrassment of the lesser circulation. In this case the latter was not reached, because the patient died of liver and renal failure before it could occur.

The bundle branch block and anginal attacks recorded during the illness would appear to be secondary to the myocardial ischaemic necrosis

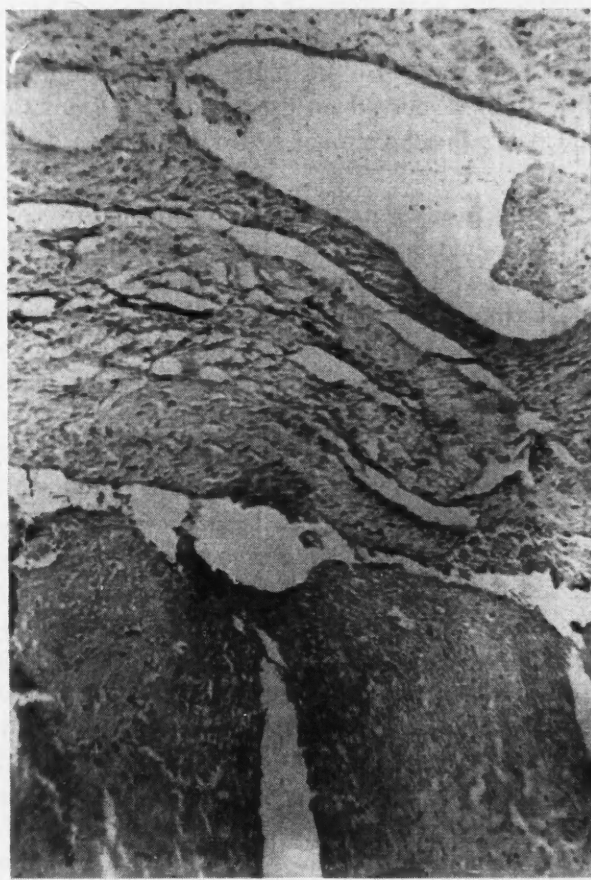


Fig. 5.—Left renal vein showing a recanalized thrombus with later fresh thrombus formation. $\times 40$.

seen on histological examination of the heart, and the persistently low diastolic blood pressure noted throughout the course of the disease is evidently related to the regurgitant factor accompanying the stenosis.

Nephrosis arising from renal vein thromboses is a rare occurrence. Blainey *et al.*² reviewed the literature and added three more cases to a very short list. They suggest that the proteinuria is due to either a high renal venous pressure or interference with the renal venous return, a view which this case supports. It is now generally agreed that the focal point of the nephrotic syn-

drome lies in the glomerulus itself, possibly due to an increase of permeability in the capillary membrane.^{5, 6, 11}

At first sight, damage to the glomerular membrane following anoxia secondary to the slow renal blood flow would appear to be a sufficient explanation for a suggested increase in capillary membrane permeability in this type of case. However, as the tubular epithelium is dependent for its oxygen supply on blood received from the afferent arteriole, glomerular anoxic damage should be reflected by changes in the tubular epithelium, an epithelium sensitive in its response to oxygen deficiency; this does not appear to be so, for in this case histological examination of the tubules showed no great variation from the normal, a finding similar to that of Blainey *et al.* in their first case.

If the proteinuria cannot be satisfactorily explained on the basis of anoxic damage to the glomerular membrane, the alternative presents itself that the nephron is relatively normal functionally, but the rate of blood flow through its vascular channels demands greater consideration.

The present concept of glomerular function appears to regard the glomerulus as a sieve, with pores of a size that retains large molecules while small pass through. However, the size of some of the pores in health must be larger than that of a molecule of albumin, for man normally excretes 30-75 mg. per day of the latter in his urine. If this view of the glomerulus is accepted—that it is a filter with some of its pores normally large enough to allow the escape of albumin—and related to changes in the velocity of glomerular blood flow, it follows that the slower the flow, the greater the number of molecules of albumin lost and vice versa. To test the validity of this idea, a fairly simple experiment was performed. A board 30 inches (75 cm.) long and 7 inches (17.5 cm.) wide had 216 long holes bored, beginning at 12 inches from one end; these holes were approximately equidistant in both directions from each other and in space occupied the lower 18 inches of the board. The holes were 3/16 inch in diameter. The board was completed by nailing a small wall in either side. Next, lead shot of 1/16 and 2/16 inch diameter were obtained and the experiments conducted by allowing the shot to roll down the board from the undrilled and over the perforated portion. The speed with which the shot rolled was regu-

lated by raising the unpunctured end from the horizontal. The shot were, as far as possible, given a standing start. With the incline at 5 degrees, about 90 large shot and 450 small fell through the sieve, at 10 degrees sixteen large and about 250 small, at 20 degrees no large and approximately 150 small and at 45 degrees no large and 4 small. The optimum velocity was therefore obtained at a 20-degree incline.

Translating this board experiment into terms of a convoluted capillary, it may be presumed that there is an optimal rate of glomerular blood flow in which small molecules will sieve out and the larger be retained; on such a hypothesis it is therefore not necessary to postulate increased capillary membrane permeability as the cause of proteinuria in this type of case. Further, it is a logical backward extension of the explanation for orthostatic albuminuria, now thought to arise from transient compression of either the renal veins or inferior vena cava.

Bell¹ has described a thickening of the capillary basement membrane in the glomerulus in nephrosis which may terminate in glomerular destruction. Duguid³ has shown that organized mural thrombi are a common cause of intimal thickening, the precursor of atherosclerosis. If the rate of blood flow through the glomerulus is slow, the basic requirement for the precipitation of platelets and fibrin to form such mural thrombi as those described by Duguid is met; it follows that organization of these thrombi will eventually lead to the histological picture described by Bell.

The only distinguishable difference between the nephrosis produced by renal vein thrombus and so-called lipid nephrosis is the inability to detect gross obstruction to the renal circulation in the latter; it would seem reasonable to postulate a similar cause but a different mechanism as the primary factor in the lipid type of disease.

Consideration of the renal circulation suggests that constriction of the efferent glomerular arteriole could produce a slowing of glomerular circulation rate. It is known that renin, an efferent arteriolar constrictor, given experimentally, will increase the glomerular filtration rate and considerably decrease renal blood flow,⁷ a condition parallel to that produced by partial blockage of the renal veins, with some modification. In health, partial stasis of the glomerular blood flow secondary to efferent arteriolar constriction could be compensated for

by afferent arteriolar constriction and increased left ventricular output; if, however, there was imbalance between efferent constriction and proximal response, the modification necessary for the production of nephrosis as suggested by this hypothesis has been made.

It would appear to follow naturally that the therapeutic response which sometimes follows such diverse treatments as malaria, measles and cortisone for nephrosis has a common basis, that is, the successful stimulus for proximal renal vasoconstriction accompanied by an increased left ventricular output, thus overcoming the effect of the distal efferent block, or alternatively relaxation at the efferent arteriole with re-establishment of the normal glomerular blood velocity.

RESERPINE IN CHRONIC PSYCHOSES*

W. FORSTER, M.B., B.S., D.P.M.,
W. SCHLICHTER, M.D. and
A. L. HENDERSON, B.Sc., Brandon, Man.

INTRODUCTION

THERE HAS ALREADY been considerable investigation of the use of reserpine in psychiatry, and this has resulted in a spate of reports. The findings in these range from the production of complete remissions in at least 25% of chronic psychotics^{1, 2} to the initiation of general tranquillity in otherwise refractory patients, making possible the abolition of restraint and the institution of occupational therapy and psychotherapy.^{3, 4}

While we were prepared to accept that the drug is in some way effective in psychotics, we were interested in investigating its effects more specifically. Principally we wished to determine its effects on individual major psychotic symptoms, regardless of the psychiatric diagnosis. We therefore set up an investigation directed towards observation of its effect on *hallucinations, delusions, activity, mood and sleep*.

*From the Hospital for Mental Diseases, Brandon, Manitoba. Supplies of reserpine (Serpasil) for this investigation were kindly donated by Ciba Company Ltd., Montreal.

SUMMARY

A case of congenital aortic stenosis complicated by stenosis of the right heart and bilateral thrombosis of the renal veins has been described. An explanation for the nephrosis arising from renal venous block has been given and, from this, a hypothesis advanced which attempts to clarify part of the mechanism responsible for lipid nephrosis.

REFERENCES

1. BELL, R.: *Am. J. Path.*, 14: 691, 1938.
2. BLAINNEY, J. D., HARDWICKE, J. AND WHITFIELD, A. G. W.: *Lancet*, 2: 1208, 1954.
3. DUGUID, J. B.: *J. Path. & Bact.*, 60: 57, 1948.
4. EAST, T. AND BAIN, C.: *Brit. Heart J.*, 11: 145, 1949.
5. FISHBERG, A. M., *Hypertension and Nephritis*, 5th ed., Lea & Febiger, Philadelphia, 1954, p. 459.
6. CHINARD, F. P. *et al.*: *J. Clin. Invest.*, Suppl. 4, 33: 621, 1954.
7. Annotations: *Lancet*, 1: 1278, 1954.
8. MAZZEI, E. S.: *Arch. cardiol. y hemat.*, 11: 173, 1930.
9. RUSSEK, H. I. AND ZOHMAN, B. L.: *Am. Heart J.*, 30: 427, 1945.
10. *Idem*: *Circulation*, 1: 759, 1950.
11. SPECTOR, W. G.: *J. Path. & Bact.*, 60: 187, 1954.

METHOD

The investigation was in two parts: a controlled pilot study followed by an intensive course of therapy in selected patients.

Results were classified as follows: The term *much improved* when applied to a symptom meant its marked amelioration or disappearance. When applied to a patient it referred to the marked amelioration or disappearance of all psychotic symptoms. *Improved*, applied to a symptom, indicated its amelioration with treatment, although the symptom itself remained. When applied to a patient, it indicated amelioration of one or more symptoms without change in the basic psychosis. The term *unimproved* is self-explanatory.

In the pilot study, 58 patients were allocated at random to treatment and control groups, given reserpine and a placebo of an identical appearance respectively. None of the staff concerned with the nursing, clinical or psychological observations knew to which groups the patients belonged. The plan of the experiment conformed to that of our previous investigations^{7, 8} except that the groups were not exchanged. Although all precautions were taken to disguise the reserpine group from the nursing staff, the flushing and drowsiness following the initial injection of reserpine in most patients were sufficient to distinguish those getting the

drug. However, this knowledge was not available to the senior author or the psychologist.

Nurses assigned to the investigation kept a continuous record of each patient on a chart designed to evaluate changes in the symptoms under study. Recording began seven days before treatment and was continued 14 days after the last dose. Every week the senior nurse also assessed each patient on the Henderson-Schultz modification of the Gardner Behaviour Chart.⁵ Eighteen patients were given Bender Gestalt and Rorschach tests before and during the experiment.

If a satisfactory psychiatric response had not been obtained by the 14th day, the dose was increased to 15 mg. intramuscularly. If a satisfactory response had been obtained, the dose was adjusted to maintain it, using oral and/or parenteral administration. Owing to the physical effects of the reserpine, most patients did not receive 10 mg. intramuscularly after the 14th day. Only one patient had 10 mg. daily for the six-week course. Response was recorded as in the pilot study. The patient's record prior to reserpine therapy was used as control.

TABLE I.

RESULTS OF PILOT STUDY						
		During treatment			2 weeks after treatment	
		Much improved	Improved	Unimproved	Improved	Unimproved
Activity.....	Placebo.....	0	2	27	1	28
	Reserpine.....	0	12	17	6	23
Hallucinations.....	Placebo.....	0	2	27	1	28
	Reserpine.....	0	7	22	2	27
Delusions.....	Placebo.....	0	1	28	0	29
	Reserpine.....	0	3	26	0	29
Accessibility.....	Placebo.....	0	2	27	1	28
	Reserpine.....	0	13	16	4	25
Mood.....	Placebo.....	0	3	26	1	28
	Reserpine*.....	0	19	10	9	20

*Statistically significant results, that is, P is less than 0.05.

Reserpine was given according to the following schedule:

Day 1: 5 mg. reserpine intramuscularly.

Days 2-6: 5 mg. reserpine intramuscularly and 2 mg. orally.

Day 7 *et seq.*: 2-5 mg. orally according to the patient's response, to a total of 4-6 weeks.

The intensive course was given to 15 cases over a six-week period as a follow-up to the pilot study. Eleven of the cases had already had reserpine therapy in that study, eight of them having shown a definite rapprochement after the initial injections, with subsequent relapse. The other four patients were hallucinated, frequently disturbed, and had not responded to electroconvulsive therapy (ECT) or insulin coma.

Treatment was as follows:

Day 1: 5 mg. reserpine intramuscularly.

Day 2: 7.5 mg. reserpine intramuscularly.

Days 3-14: 10 mg. reserpine intramuscularly.

RESULTS

The pilot study.—The physical effects seen were: (a) A significant mean decrease in pulse rate of 10 beats per minute for the reserpine group compared with an insignificant change (plus 1 per minute) in the controls. (b) A fall in blood pressure in 28 of the 29 reserpine patients: a mean decrease for the group of 12 mm. systolic and 11 mm. diastolic compared with the pre-treatment average. There was no significant change in the placebo group. (c) No physical reactions to the placebo. On injection of reserpine 27 patients flushed, 10 had tremors, and 21 became drowsy. With oral medication 14 showed no reaction, 7 became pale, 2 had drooling in the 5th week, and 6 continued drowsy throughout the course.

There was no effect on the patients' usual length of sleep, but one patient developed insomnia. When a patient appeared to be asleep following administration of reserpine, he could easily be aroused and generally denied he had been sleeping. E.E.G. records on patients "sleep-

ing" after reserpine are not those of normal sleep, and reserpine might even prevent deep sleep.⁶

The mental changes are shown in Table I. Only the results with respect to mood are statistically significant for the reserpine group. No specific effect was seen on the basic content of the psychosis.

The change in mood was quite distinctive, however. There was better rapport between patient and patient, and patient and staff. Irritable patients became more tolerant. Those hostile because of their delusions became less so, although the delusions were retained.

standing delusions in one case. Three patients were considered much improved, nine improved. Relapse after treatment was, however, the rule. Only one patient remained much improved and was able to be discharged; five maintained a level of improvement, and nine showed relapse to their original status.

The effect on individual symptoms is shown in Table II. As with our pilot study, the main effect was the induction of rapprochement and an easier attitude of the patient towards his delusions. The structure of the psychosis was not changed except in Case A reported below. Three case histories are as follows:

TABLE II.

INTENSIVE TREATMENT WITH RESERPINE						
Doses up to 15 mg. by injection daily for 14 to 42 days followed by oral doses when indicated.						
	During treatment			2 weeks after treatment		
	Much improved	Improved	Unimproved	Much improved	Improved	Unimproved
Activity	3	8	4	1	4	10
Hallucinations	1	3	10	0	2	13
Delusions	2	0	13	1	0	14
Accessibility	2	8	5	1	2	12
Mood	3	9	3	1	5	9
Patients	3	9	3	1	5	9

The hospital psychologist, Mr. Neil Hildebrand, B.A., reported: "Eighteen cases were tested, nine from each group. An initial study indicated the Bender Gestalt and Rorschach tests as most suitable for the type of patient selected. Reaction time and total production time received special consideration.

"At the termination of the investigation it was found that test results alone did not suffice to distinguish significantly between treated and untreated groups. Test-retest comparisons also did not show any fundamental changes in psychosis or personality. It was noted, however, that the treated group was more subdued both in motor and bizarre-ideational activity. In relation to the latter, there was a definite decrease in spontaneity of verbalization. However, when the patient was pressed to make further associations to the Rorschach responses, he produced bizarre associations similar to those present on pre-treatment testing."

The intensive course.—During treatment, all but three of the patients showed improvement, which ranged from lessening of tension to the apparently complete disappearance of long-

CASE A

A 40-year-old single woman had been in hospital continuously since 1953, showing grandiosity combined with fantastic delusions. She stated that she was 200 years old, had four sets of teeth and more than 100 children. She was still having children when 80 years old. She stated she was a nurse, teacher, doctor, lawyer, minister, singer, lion-tamer and arctic explorer: due to her, the trans-Canada railroad had been completed. She took no interest in her surroundings, avoided other patients, had a critical and sarcastic attitude, and claimed the staff were trying to harm her. ECT and insulin were ineffective.

She received reserpine during the pilot experiment, showing marked improvement in attitude while receiving injections but relapsing on oral medication.

She was then given the intensive course, on which she developed mild Parkinsonian signs. On the 11th day she was co-operative and friendly. By the 21st, she showed signs of questioning her delusions. At this point Parkinsonian symptoms were marked and from the 30th day she was given only 3 mg. orally per day. By the 47th day she appeared to have lost all her delusions. She described the subjective effects of her treatment as follows: "The drug reduced me to infancy—I could not use my hands because they lost strength and were clumsy. It took me five times longer to put on my dress. When I was smoking, I could hardly find my mouth, the same with eating—another patient had to find my mouth for the spoon . . . I couldn't read because I couldn't concentrate—I felt very restless—when I was on the heaviest dose I couldn't sleep because of the tremblings. I worried about getting through the treatment. I didn't care about the rest of the world—my ideas [delusions] didn't seem to matter as I thought I was going to die."

At the termination of treatment she denied her delusions, although her evasiveness at times suggested

they might be more suppressed than completely absent. She was sociable and co-operative, not in the least grandiose, made rational plans for her future and was discharged.

CASE B

A 49-year-old male had been in hospital since 1951, continuously paranoid and aggressive in manner and constantly hallucinated in the somatic and auditory fields. On one occasion he smashed the ward radio because of the abusive voices from it. He made transient improvement with insulin, none with ECT. He was without insight, and resented his incarceration and being questioned about his delusions and hallucinations.

Before any investigation, he received reserpine in doses of up to 2 mg. orally daily, and on this he showed a marked improvement in attitude, becoming quite approachable, friendly and ready to discuss his condition, though without basic alteration in his psychosis. When reserpine was discontinued he relapsed to his previous state.

During the pilot study he received placebo and showed no changes whatever.

On intensive therapy he again showed marked improvement and his somatic hallucinations disappeared. By the end of the second week, he was much more pleasant and co-operative, though his delusions persisted. He maintained this level for about a month after cessation of therapy, then relapsed.

CASE C

A 40-year-old male had been continuously in hospital since 1942. He was withdrawn, with schizophrenic thought disorder and mood impairment, ideas of influence, and frequent auditory hallucinations with consequent behaviour disturbance. He had shown transient improvement with insulin, none with ECT.

In the pilot study he received reserpine and improved noticeably in rapport (although the delusions and hallucinations were unchanged) while on 5 mg. daily by injection. He relapsed on oral medication. Given the intensive course he became apprehensive, his delusions were aggravated and he showed marked Parkinsonian features. Dosage was reduced to 3 mg. orally daily on the 20th day. On this he showed a slight improvement over his pre-treatment status, but relapsed when medication was stopped.

PHYSICAL REACTIONS

Physical reactions were obvious in most cases. The characteristic complaint in 10 patients was of tiredness of the leg muscles, together with a paradoxical feeling of restlessness that made them want to move around. Symptoms of Parkinsonism were frequent with higher doses, but subsided when the drug was withdrawn for three days and subsequently given in smaller amounts.

One patient, originally selected, showed hypersensitivity to the drug. He had a history of asthma. Two hours after 5 mg. reserpine intramuscularly, he developed nausea, vomiting and dyspnoea which required oxygen. All symptoms cleared within four hours of their onset, but reserpine treatment was not continued.

DISCUSSION

When the experiment was initiated, we hoped to establish the effect of reserpine on individual psychotic symptoms with the secondary goal of finding indications for its use in specific psychoses of a chronic type. In the latter respect the experiment has been unsuccessful; the results did not suggest a basis for the clinical selection of patients for treatment. They do show, however, that while delusions and hallucinations persisted with the same content, there was a significant improvement in rapport and more subdued behaviour in a significant number of cases.

The most consistent initial improvement was seen in catatonic schizophrenics, all of whom relapsed about two weeks after the drug was withdrawn. The most *useful* improvement was seen in irritable paranoids who became more pleasant and manageable on treatment, but who also relapsed on its termination. Possibly, in these cases, a "total push" therapeutic programme added to the reserpine therapy might have produced a greater or more lasting improvement, but our purpose was to evaluate the effect of the reserpine without complicating the picture. Nevertheless, the rapprochement achieved as a direct effect of the drug is of undoubted value in mental hospital practice, whether as an ancillary to other methods of treatment or simply to produce pleasanter wards. Consequently its long-term use in chronic psychotics is justifiable.

Our results do not provide any firm guide as to dosage. Apart from Case A, no more sustained improvement was seen after intensive parenteral therapy than after smaller parenteral or oral doses. In fact some patients, as in Case B, showed as much improvement after small doses of 1 to 3 mg. orally daily as on high doses.

In our pilot study, reserpine did not markedly alter delusions and hallucinations in a significant number of patients. On the other hand, one must consider the reactions of the individual patient as well as statistics. As shown by the rapprochement on the wards and by the projective techniques of the psychologist, while the basic content of the psychosis was unchanged, the overt and disturbing psychotic manifestations began to be of less importance.

Case A illustrates in our opinion a definite response to reserpine. A case of this type might, of course, improve spontaneously, though this

would be uncommon. Or improvement might occur from some extraneous, unknown factor, or as a result of the psychic reaction to the sensations induced by the drug—which in the case reported actually produced fear of death. However, the pattern of improvement with parenteral therapy during the pilot study, relapse on withdrawal and continued and sustained improvement with intensive therapy points to a direct effect of reserpine.

We did not see a "turbulent phase" in any of our patients, though some showed restlessness and agitation. Continued therapy in these cases did not produce any better result than in those who showed none.

It seems to us that reserpine therapy is analogous to insulin coma therapy from the aspects of patient selection and depth of treatment. It is generally conceded that all schizophrenics should have insulin therapy on their first admission, since selection on a clinical basis is unreliable. Similarly, just as some patients require deep comas or a large number of comas before improving, so some patients may require high doses of reserpine or a prolonged course of treatment.

In general, we believe that reserpine administration in chronic psychoses falls into much the same category as the shock therapies, and that for the majority of cases its sphere will be that of a valuable maintenance treatment.

SUMMARY AND CONCLUSIONS

The effect of reserpine on hallucinations, delusions, activity, mood and sleep in chronic psychoses was studied: (a) in a controlled pilot experiment, and (b) in an intensive course of treatment. In the pilot study, 29 patients were treated with 5 mg. reserpine daily parenterally for 6 days followed by oral doses of up to 5 mg. daily to a total of 4 to 6 weeks. A control group of 29 patients received a placebo. In the intensive course, 15 cases were treated for 6 weeks with doses of up to 15 mg. parenterally daily.

The drug produced a statistically significant and striking alteration in mood, seen as rapprochement between patient and patient, and patient and staff. Irritable patients became more tolerant and deluded patients less hostile. Despite this, there was no change in the basic content of the psychosis and no statistically significant effect on hallucinations, delusions or sleep.

The results did not give a guide for patient selection or preferred dosage. Some patients improved as much on a relatively small dose (1 to 3 mg. orally daily) as on a high dose.

Reserpine therapy in chronic psychoses is comparable to shock therapies, its main (and valuable) application being as a maintenance therapy. Only one patient out of the 15 treated intensively recovered enough to leave hospital. The majority of cases relapsed after cessation of therapy.

The authors wish to express their appreciation to Dr. Stuart Schultz, Superintendent of the Hospital for Mental Diseases, Brandon, Manitoba, without whose assistance and support this investigation could not have been carried through, and the members of the staff of the Brandon Hospital for Mental Diseases who carried out the many and varied tasks necessary for an investigation of this type.

The investigation was carried out as part of project 606-5-67 supported by a National Health Grant.

REFERENCES

1. BARSA, J. AND KLINE, N.: *Am. J. Psychiat.*, in press.
2. NOCE, R. H., WILLIAMS, D. B. AND RAPAPORT, W.: *J. A. M. A.*, 158: 11, 1955.
3. BLEULER, M. AND STOLL, W. A.: *Ann. New York Acad. Sc.*, 61: 167, 1955.
4. SAINZ, A. A.: *Ibid.*, 61: 72, 1955.
5. SCHULTZ, S. AND EVANS, H. S.: *Manitoba Med. Rev.*, 33: 243, 1953.
6. MONROE, R. R. *et al.*: *Ann. New York Acad. Sc.*, 61: 56, 1955.
7. FORSTER, W., SCHULTZ, S. AND HENDERSON, A. L.: *Geriatrics*, 10: 26, 1955.
8. *Idem*: *Canad. M. A. J.*, 72: 678, 1955.

CONTROLLED TRIALS

"One of the weaknesses of scientific medicine is that it teaches cold detachment to young physicians while they perform so-called controlled trials. But a good doctor can never become detached from his patients' problems. His duty, according to Clifford Allbutt, is occasionally to cure, sometimes to alleviate, but always to comfort. It is fitting to find at last that the controlled trials are not controlled because even the detached modern physician evokes the unwanted placebo reaction. Knowing about this should not make us disbelieve in our favourite remedy. We should apply it with greater enthusiasm and get better results. It should also make us more tolerant if other doctors claim good results for remedies which will not work for us."—A letter in *M. J. Australia*, 2: 264, 1955.

THE DIAGNOSIS AND TREATMENT OF ACUTE PYELONEPHRITIS IN DIABETES MELLITUS*

GUY E. JORON, M.D.,
A. F. FOWLER, M.D.,
JOAN DE VRIES, M.D.,
GRANT REID, M.D. and
W. H. MATHEWS, M.D., *Montreal*

IT HAS BEEN WELL established that pyelonephritis is a common and serious complication of diabetes mellitus. The incidence of pyelonephritis at post-mortem examination is reported as 18-22% in diabetics as compared with 3-4% in non-diabetics.¹⁻⁵ In fact, the characteristic nephropathy of long-standing diabetes is a mixed lesion showing arteriosclerosis, hyaline deposits and some degree of pyelonephritis. In addition, the pathologist not uncommonly finds in diabetics that a clinically unsuspected acute pyelonephritis was the principal cause of death. As in many of these cases the diagnosis was not made during life, it would seem reasonable to infer that the commonly taught signs and symptoms of acute pyelonephritis are not reliable when this condition develops in a diabetic. The purpose of this paper is to report on observations of 23 diabetics with acute pyelonephritis in an attempt to establish criteria for the early recognition of this condition and to describe its treatment.

Acute pyelonephritis in a diabetic is a condition fraught with the greatest danger. Like any other infection it can precipitate diabetic coma, with the added hazard that the impairment of renal function may make the acidosis more severe and more difficult to correct. It can be met with in the usual situations where it is wont to occur in non-diabetics, as in pregnancy, and with the same manifestations. But the most common and serious form of acute pyelonephritis which is encountered in diabetics and to which we wish to call attention presents in a surreptitious manner without the complete classical picture of chills, rigors, acute loin pain and tenderness in the costovertebral angle, high spiking fever and burning urination. If untreated, the condition usually ends fatally within one

or two weeks. Renal medullary necrosis or necrotizing papillitis is a common complication.

ANALYSIS OF 23 CASES OF DIABETES MELLITUS WITH ACUTE PYELONEPHRITIS

Analysis of our cases shows that acute pyelonephritis occurred predominantly in the older age group. Thus 19 patients were over the age of 60. The sex distribution—14 women and 9 men—probably reflects the preponderance of diabetes in women. Fourteen patients survived and nine died; of the latter, eight came to autopsy. In five of these eight cases a diagnosis of acute pyelonephritis had been made during life. In the remaining three this clinical diagnosis had been considered and then rejected because of insufficient evidence. The post-mortem examination, however, revealed that pyelonephritis had indeed been the principal cause of death.

The presenting complaints (on admission) are listed in Table I. The most common were

TABLE I.

<i>Presenting complaints</i>	<i>No. of cases</i>
Nausea and vomiting	12
Fever and chills	8
Delirium and confusion	7
Drowsiness	5
Weakness	5
Loin pain (dull)	3
Chest pain	2
Abdominal pain (generalized)	2
Burning on urination	3
Frequency of urination	3
Incontinence of urine	3
Dysuria (vague)	1
Anuria	1
Pruritus vulvae	1

nausea and vomiting followed in order of frequency by other systemic symptoms such as fever and chills, delirium, confusion, drowsiness and weakness. Pain was never a prominent feature and was never acute. Only three patients mentioned pain in the loin.

Urinary symptoms were not striking. When they did occur, they could be easily interpreted by the patient or physician as due to poor control of the diabetes.

On physical examination abnormal signs were few. They are listed in Table II. None had acute pain on pressure in the costovertebral angle. In only two could we demonstrate any tenderness in the loins. In four cases there was slight to moderate tenderness on palpating the abdomen. Abdominal distension was noted in

*From the Departments of Metabolism, Bacteriology, Urology and Pathology, the Montreal General Hospital and McGill University, Montreal, Canada. Supported by grants from the Banting Research Foundation. Presented at the Joint Meeting of the British Medical Association, Canadian Medical Association and Ontario Medical Association, Toronto, June 1955.

TABLE II.

PHYSICAL SIGNS	
Tenderness on palpation (slight to moderate):	
Abdomen.....	4 cases
Loin.....	2 "
Scapular area.....	1 "
Suprapubic area.....	1 "
Abdominal distension.....	3 "
Cedema of the legs.....	2 "

NOTE:—All patients looked very ill, to a much greater degree than could be explained by the physical findings.

three. Two had dependent oedema which regressed with treatment of the pyelonephritis. The maximum temperature in the first 24 hours varied between 98.4° F. and 104.1° F. An important point is that the patient looked seriously ill in spite of the paucity of physical signs. One had the impression that the degree of illness was more marked than could be explained by the physical findings.

TABLE III.

LABORATORY FINDINGS		
	Absent	Present
Urine Glucose.....	14	9
Ketone bodies.....	21	2
Protein.....	14	9
	<i>0-Few</i>	<i>Elevated</i>
Red cells.....	19	4
White cells.....	6	17
	<i>Normal</i>	<i>Elevated</i>
Blood urea nitrogen.....	4	19
White cell count.....	Usually 10,000-15,000	

Pertinent laboratory findings are recorded in Table III. The chemical tests on the urine were not helpful. Microscopic examination of the urine may be misleading since pyuria is not always present. The results shown in the tables are those of the admission urinalyses. Although in all our cases the urine contained an abnormal number of pus cells on at least one occasion, it is important to note that in about one-quarter pyuria was not found on the first examination. The blood urea nitrogen level was usually elevated to two to three times the normal value. A leukocytosis of 10,000 to 15,000 was the rule.

When the clinical picture described appears, a diagnosis of acute pyelonephritis should be entertained and this possibility investigated by culture of a catheter specimen of urine. The results of the original urine culture in each patient are listed in Table IV.

TABLE IV.

ORIGINAL URINE CULTURES	
<i>E. coli</i>	9
<i>Staph. pyogenes</i>	4
<i>Proteus</i>	2
<i>Pseudomonas</i>	1
<i>Strep. zymogenes</i>	1
<i>A. aerogenes</i>	1
Mixed.....	5

PITFALLS IN DIAGNOSIS

Our experience has shown that the common pitfalls in diagnosis are confusion with diabetic acidosis, a cerebrovascular lesion or a surgical intraabdominal lesion and exclusion of the diagnosis of acute pyelonephritis because pus is not found in the urine.

Drowsiness in a diabetic always raises the possibility of diabetic coma, particularly when it is associated with nausea and vomiting. The laboratory findings may also simulate those in diabetic acidosis. Thus infection will aggravate the diabetes-producing glycosuria; nausea and vomiting will lead to ketonuria; and acidosis may result from impaired renal function. Indeed both pyelonephritis and diabetic coma may be present. In attempting to distinguish between these conditions it is useful to remember that acute pyelonephritis is encountered chiefly above the age of 60 years when diabetic coma seldom occurs. Also, Kussmaul respiration—a cardinal sign of diabetic coma—is rarely seen in the acidosis associated with acute pyelonephritis.

Drowsiness with confusion may be present in acute pyelonephritis and be wrongly interpreted as indicating a cerebrovascular lesion.

The pain in our cases was not sharply localized and never severe. Commonly a smouldering surgical intraabdominal lesion was suspected. We cannot explain why the pain was never in the costovertebral angle and was more often demonstrated anteriorly. Intestinal obstruction, cholecystitis and diverticulitis were suggested diagnoses. It may be impossible to distinguish an acute pyelonephritis from an acute surgical intraabdominal lesion with coexistent chronic asymptomatic pyelonephritis.

Another error is to rule out the diagnosis of acute pyelonephritis because pus is not found in the voided specimen of urine. Many elderly diabetics have a relaxed bladder floor due to a cystocele or prostatic hypertrophy. There may

be bladder atony due to diabetic involvement of the autonomic nervous system. When such patients are confined to bed they may void relatively clear supernatant urine, whereas the terminal portion of a catheter specimen might be loaded with pus. Cases have been seen where even catheter specimens have been clear. In such instances repeated specimens should be examined if the clinical suspicion is sufficiently strong.

TREATMENT

The chances of recovery from acute pyelonephritis in diabetes are greatly increased by early and intensive antimicrobial therapy. The antimicrobial agent of choice is obviously one to which the offending organism is sensitive. Therapy should be instituted as soon as the diagnosis is made or suspected and should not await the results of the urine culture and sensitivity tests. It is therefore preferable to choose an agent which is likely to be effective against the common urinary pathogens as well as the organisms which usually grow when the original sensitive organisms have been suppressed.⁶⁻⁸ These patients are an easy prey to secondary infections, usually by species of *Proteus*, *Pseudomonas* or types of staphylococci. We have found that Chloromycetin* (chloramphenicol) offers the best chance of success, and it is more likely to clear the infection with the first intensive course of treatment. We give two to four grams a day by intramuscular injection for the first week and half that dose for the second week. We have seen no toxic effects.

If the organism is sensitive, there will usually be a marked improvement in the patient's sense of well-being and appearance within 48 hours and before there is any laboratory evidence of improvement. We repeat the culture and sensitivity tests on a clear voided specimen of urine two or three days after beginning treatment, even though the patient may be improving because a change in flora may be taking place. A change of organism should be watched for carefully and treated intensively with the appropriate antimicrobial agent. Any sudden regression in the patient's condition with recurrence of fever should be interpreted as evidence of a change in the bacterial flora of the urinary tract demanding a change in drug.

*We wish to thank Parke, Davis & Company, Ltd., for their generous gift of Chloromycetin used in this study.

It is rather difficult to decide on the duration of treatment. We have rather arbitrarily chosen two weeks. At the end of this time most patients either have clear urine or still have pus and bacteria in the urine without other clinical evidence of disease. The majority do not relapse after stopping treatment, even though pus and bacteria persist in the urine. Under these circumstances it is better to leave well enough alone, and further antimicrobial treatment is not given. If there is a clinical relapse, appropriate antimicrobial therapy should be resumed.

Many of these patients develop a marked secondary anaemia. Correction of the anaemia with whole-blood transfusions will assist in overcoming the infection.

The results of treatment are gratifying if we consider that we are dealing with a condition which in most cases would otherwise be fatal. Further improvement in results will depend upon earlier recognition of this disease and investigation of the factors which make the diabetic so susceptible to urinary-tract infection.

SUMMARY

Acute pyelonephritis is a serious complication of diabetes and is often unrecognized.

Clinical and laboratory findings in 23 diabetics with acute pyelonephritis are reported in an endeavour to delineate the clinical picture of this condition.

Attention is drawn to the fact that the symptoms and signs are largely systemic and not localizing.

Pitfalls in diagnosis are discussed.

Early and intensive antimicrobial therapy has given good results. Intramuscular chloramphenicol in doses of 2-4 g. a day is recommended.

REFERENCES

1. BALDWIN, A. H. AND ROOT, H. F.: *New England J. Med.*, **223**: 244, 1940.
2. SHARKEY, T. P. AND ROOT, H. F.: *J. A. M. A.*, **104**: 2231, 1935.
3. ROBBINS, S. L. AND TUCKER, A. W., JR.: *New England J. Med.*, **231**: 865, 1944.
4. OPHÜLS, W.: A statistical survey of three thousand autopsies from the Department of Pathology of the Stanford University Medical School, Stanford University Press, University Series, *M. Sc.*, **1**: 127, 1926.
5. EDMONDSON, H. A., MARTIN, H. E. AND EVANS, N.: *Arch. Int. Med.*, **79**: 148, 1947.
6. JORON, G. E. *et al.*: *Diabetes*, **4**: 99, 1955.
7. JAWETZ, E.: Urinary tract infections. Disease-a-month Series, November 1954, The Year Book Publishers Inc., Chicago.
8. FLIPPIN, H. F. AND EISENBERG, G. M.: Antimicrobial therapy in medical practice, F. A. Davis Co., Philadelphia, 1955.

TREATMENT OF THE NEPHROTIC SYNDROME IN CHILDREN*

C. P. RANCE, M.D., F.R.C.P.[C.] and
A. L. CHUTE, M.A., M.D., Ph.D.,
F.R.C.P.[C.], Toronto

AS SEEN IN ADULTS the nephrotic syndrome, consisting of oedema, proteinuria, hypoproteinaemia, hyperlipaemia occurs most commonly as a stage in the relentless progressive course of chronic nephritis and carries an almost hopeless prognosis. The situation in children is quite different, and the majority of children who are seen with a nephrotic syndrome follow a clinical course which resembles that of "pure lipoid nephrosis". At present, the term "nephrotic syndrome of undetermined etiology" is usually used, thus excluding a nephrotic syndrome which may occur in the course of other diseases such as lupus erythematosus, syphilis, amyloid disease involving the kidney, or as a result of renal damage from poisons such as mercury, or drugs such as trimethadione (Tridione).¹ This term also allows the inclusion of children who may have transient periods of hypertension, azotemia and even gross haematuria, as it has been found that these signs do not make recovery less likely.² The disease is much commoner in younger than in older children or adults, and has even been described as commencing in the first month of life.³

Its etiology is unknown, though there is much evidence that an antigen-antibody reaction affecting chiefly the glomerular basement membrane is an important factor. What the antigen is, and why certain children react for a time in this way, are questions still to be answered.

The onset is usually a fairly rapid appearance of oedema which becomes generalized and severe, and includes ascitic and less often pleural effusions. The child becomes irritable, listless, and anorexic. Oliguria is present, and the urine will contain much protein and many casts, with or without microscopic haematuria. A high serum total lipid and cholesterol are found, and a low serum protein and albumin. Although spontaneous remissions may occur, the child may remain very oedematous for months at a time, with periods of anorexia, diarrhoea, vomiting, and

semi-invalidism to complete invalidism because of oedema. Another distressing and dangerous aspect of the disease is the extreme susceptibility to infections, which is attributed to the abnormally low serum gamma globulin. While some infections aggravate the disease, other infections may actually lead to a remission of the disease. About 50% of the patients ultimately recover after one to three years, and they remain well thereafter. The remainder may die of infection or pass on to a stage of progressive renal destruction and insufficiency.

Until recent years, treatment of the nephrotic syndrome was purely symptomatic. In the past five years, methods of therapy have been developed which appear to attack the underlying disease itself, resulting in complete remissions. At first such remissions were usually only temporary, but ways are now being found to prolong them, with the hope that in many cases they will be permanent. Remissions may be induced by treatment with ACTH, cortisone, or nitrogen mustard.⁴ We have had no personal experience in the use of nitrogen mustard, and it will not be discussed in this paper. At times treatment with hormone is inadvisable or contraindicated, and then a knowledge of the symptomatic treatment is most important. The remainder of this paper will deal with both forms of therapy.

A. GENERAL AND SYMPTOMATIC TREATMENT

1. *Rest.*—Bed rest is advisable at the onset of the disease, during infections and periods of severe oedema. At other times the children may be allowed up, but over-tiring or chilling should be avoided.

2. *Diet.*—A low-sodium normal protein diet is advised. In the presence of severe oedema the sodium intake should be as low as possible, and this can be achieved by avoiding sodium-containing foods, using salt-free bread and butter, and Lonalac* in place of milk. This is very rarely necessary, however, and most children do well on a diet in which obviously salty foods are avoided, and no salt is used in the cooking. Because large amounts of protein may be lost daily in the urine, the protein intake should be at least normal for the child's age. A multiple vitamin supplement is given, preferably one containing iodine, to make up for the lack of iodine which is normally obtained as iodized salt.

*From the Department of Pediatrics, University of Toronto, and the Research Institute of the Hospital for Sick Children, Toronto, Canada.
Aided by a grant from the National Research Council of Canada.

*Lonalac is a powdered milk from which the sodium has been removed by dialysis, made by Mead Johnson and Company Limited.

3. *Infection*.—Antibiotics have greatly reduced the mortality due to infection, but infections are still dangerous to the nephrotic child, and in the past year two children have died from infection. Each was admitted to hospital in moribund condition and died within a few hours, one from peritonitis and the other from meningitis.

Mild infections should be given careful attention, with bed rest and antibiotic therapy to prevent complications. We have tried continuous antibiotic prophylaxis through the winter months but have not been able to prove it helpful. It should be considered when there are other children in the family who might bring infections from school.

Special mention might be made of two serious infections which are particularly common in nephrotic children. The first is peritonitis, which may occur when ascites is present. There is a rapid onset of fever, vomiting and abdominal pain. The entire abdomen is tender, but it is not rigid. The white cell count is elevated, and a blood culture may reveal the pathogen. *E. coli* is the commonest cause, but pneumococci or other organisms may be found. Laparotomy is rarely necessary, but if there is localized tenderness in the right lower quadrant it is safer to operate and remove a normal appendix than to wait and have an inflamed one perforate. We have used combined intramuscular penicillin and streptomycin in the past few years, and find it quite successful in relieving pain and fever within 24-48 hours.

The second common severe infection is a cellulitis of the skin and subcutaneous tissue. This, too, starts suddenly with fever and vomiting, and on examination a tender red area of skin will be found, usually over the lower abdomen, flank or thigh. The inflamed area has a sharp but not a raised margin, and may spread rapidly till it covers a wide area. Again a positive blood culture may be found, and the infection responds well to combined intramuscular penicillin and streptomycin.

4. *Edema*.—In most nephrotic children now, edema is cleared coincidentally with hormone therapy which has been aimed at the disease itself. However, when hormone treatment is contraindicated or ineffective, edema may be so severe that it causes striæ in the skin, through which edema fluid may leak or bacteria enter. Localized collections of fluid, such as large peri-

toneal, pleural or scrotal effusions, may also require immediate treatment.

With severe edema the child should be kept at rest and on a strict low-sodium diet. Fluids may be restricted to known losses plus estimated insensible water loss.

When severe ascites is present there are at least three dangers: (1) peritonitis; (2) elevation of diaphragm with collapse of lung bases; (3) interference with renal function. A good site for abdominal paracentesis is in the midline halfway between umbilicus and pubis. There is little danger of touching the bladder, though the child should be asked to void if he can before the procedure is started. Then about 2/3 the estimated volume of ascitic fluid should be withdrawn, and a sterile dressing pad and a tight abdominal binder applied to prevent too sudden release of pressure. With this method there is frequently a continuing loss of fluid through the opening, and much edema fluid may be mobilized from the peripheral tissues and lost. Occasionally a true diuresis follows relief of a tense ascites. Antibiotic prophylaxis is given as long as drainage continues.

A large pleural effusion may embarrass respirations and heart action. It may diminish when the accompanying ascites is drained, but if necessary a thoracentesis should be done.

Scrotal swelling may be extreme and cause great discomfort. Some help is provided by supporting the scrotum with a pad or sling between the legs. We have found application of dressings of saturated solution of magnesium sulphate in glycerin to be effective in relieving the swelling.

Another way to relieve edema is to attack one of the most important causes, the low serum osmotic pressure due to low serum albumin. Infusions of salt-poor albumin can be given, but are expensive and require to be repeated almost daily, as the albumin is rapidly lost in the urine. Since the last war, dextran has become available, and has been standardized so that it has a molecular weight near that of albumin.

We have used a 6% salt-free dextran solution in six children with varying effect. The most successful result was obtained in a 2-year-old child with massive edema, weeping areas of skin, and hypertension. He was given 150 c.c. dextran one day, and three days later 200 c.c. Within a few hours of the first injection a diuresis commenced, and in six days he lost most of his edema. He was then treated with cortisone and had a com-

plete remission of his nephrotic syndrome. A 5½-year-old girl had a good result when dextran was first given, but the oedema returned at once and was not relieved by later infusions of dextran. A 4½-month-old infant received two infusions of 50 c.c. dextran six days apart, but as her tense ascites obliged us to do two abdominal paracenteses, through which much fluid drained, it was impossible to say how much of her loss of oedema could be attributed to dextran.

Two other children had no benefit from dextran, even though in one a blood dextran level of 2.0 g. % was reached. A sixth child, an 8-year-old boy, suddenly went into a state of anaphylactic shock after receiving a few cubic centimetres of his first infusion of dextran. He was revived with adrenaline and artificial respiration, was given no further dextran, and subsequently lost all his oedema following a course of ACTH. Some authors have reported more successful results with dextran,⁵ but it would seem to have the greatest value in a severely oedematous child in whom hormone treatment as described below may be contraindicated or ineffective.

5. *Immunization.*—We have seen the disease commence shortly after a smallpox vaccination, and in two children who were in remission there was a flare-up of the disease immediately following a diphtheria toxoid injection. An exacerbation occurred in another child following an injection of anti-tetanus serum. Hence it is safer to defer such immunizations till the child has been well for a year or more.

B. TREATMENT WITH ACTH AND CORTISONE

In the Hospital for Sick Children, an investigation into the use of ACTH and cortisone in the treatment of children with the nephrotic syndrome was begun by one of us (A.L.C.) in 1950 and continued to March 1954, under a grant from the National Research Council. During this time 88 children with the disease were treated. Used initially in short courses (4-6 days) because it was known that a sodium diuresis occurred on withdrawal, it was found that a remission might be produced, and that diuresis might commence even while the hormone was being given. A summary of our experience with this group of children follows.

Children were observed for a control period of several days, to ensure that they were free

of infection and hypertension, as these are considered contraindications to hormone therapy. Also no child was treated who was thought to have entered the progressive irreversible stage of the disease. Daily weight and blood pressure readings were made, and the blood non-protein nitrogen, creatinine, sodium, potassium, chloride, cholesterol and serum protein levels and albumin/globulin ratio were determined. The chemical determinations were repeated weekly or more often when indicated. The blood haemoglobin value, white cell count and erythrocyte sedimentation rate were taken before, during and after therapy. The children were kept in bed, on a diet of normal protein content, but with sodium chloride intake restricted to about 0.5 g. a day.

ACTH (Connaught Laboratories) was given intramuscularly 6 hourly in daily dosage of 20-50 mg., the dosage being adjusted so as to keep the total eosinophil count at or near zero. In older children, ACTH was given intravenously, 10-20 mg. daily in 5% glucose in distilled water, over a period of at least 8 hours.* Cortisone was given either by mouth or intramuscularly 6 hourly in daily dosage of 100-300 mg. Blood pressure readings were made before each dose, and if hypertension developed the daily dose was lowered. Mild infections were treated with antibiotics, but if a severe infection occurred the hormone was stopped.

The treatment was continued for 2-4 weeks. Frequently, diuresis commenced while therapy was still in progress, in which case treatment was continued until proteinuria disappeared or until further improvement ceased. If there was no loss in weight, therapy was stopped after two weeks, and often diuresis commenced within a few days.

When it was observed that some children had an apparently complete remission following treatment, i.e. complete disappearance of oedema and proteinuria and return to normal values for the serum proteins and cholesterol, it was concluded that the hormones had a beneficial effect on the disease itself, whatever its nature might be. This led us to try the effect of the hormones on children in whom proteinuria had recurred but who were free of oedema, and good results were again obtained.

*We have lately used a long-acting form of ACTH, Duracton (Nordic Biochemicals Limited) and find 0.50-1.5 c.c. (10-30 units) once daily is effective.

COMPLICATIONS OF HORMONE THERAPY

The commonest complication has been hypertension, which was accompanied in a few cases by convulsions. There was less tendency to hypertension when using cortisone than with ACTH.

The next most serious complication is infection, to which these children have an even greater susceptibility while under therapy. On several occasions we have felt obliged to stop hormone treatment because of the development of bronchitis, pneumonia, peritonitis, cellulitis or severe diarrhoea. Infections have developed even in children who were being given prophylactic antibiotics.

of death being evident at autopsy, although considerable hydrothorax was found.

RESULTS

1. Remissions resulting from ACTH and cortisone

The 88 children treated in this series were given 164 courses of hormone (142 ACTH and 22 cortisone). Each child received from 1 to 6 courses of treatment and, as each child may have had different results from different courses, we have shown the results in terms of individual courses. In Table I the patients have been divided into 5 groups, according to whether they were oedematous (groups 1-3) or free of

TABLE I.

ACTH AND CORTISONE THERAPY OF NEPHROTIC SYNDROME IN CHILDREN.
SUMMARY OF RESULTS OF INDIVIDUAL COURSES.

Group	Clinical classification of patients		Courses of ACTH	Courses of cortisone	Total courses
	Before therapy	After therapy			
1	Oedematous	Oed-free, Prot-free*	44	5	49
2	Oedematous	Oed-free	31	7	38
3	Oedematous	Unchanged	34	9	43
4	Oed-free	Prot-free	25	1	26
5	Oed-free	Unchanged	8	0	8
Total courses			142	22	164

*Oed-free means complete absence of oedema.

Prot-free means absence of proteinuria by qualitative tests.

The third complication is a disturbance of acid-base and electrolyte balance, most frequently a low serum potassium with metabolic alkalosis or a low serum sodium. Clinically one observes weakness, listlessness, and cardiac irregularities, and certain changes in the electrocardiogram may be found. We have not given a potassium salt as a routine measure to every child on hormone therapy, because in some oliguric children the serum potassium tends to rise. The safest procedure is to determine the serum electrolytes once or twice a week, or whenever any suggestive signs appear, and to give sodium or potassium salt as indicated.

There have been two deaths attributable to therapy. One patient, a five-year-old girl, developed hypertension, convulsions, low serum sodium and potassium, thrush, enteritis, and cellulitis, and died 17 days after treatment was stopped. The other, a 19-month-old boy, died suddenly after five days of treatment, no cause

of death being evident at autopsy, although considerable hydrothorax was found.

oedema (groups 4 and 5) before treatment, and according to the results obtained.

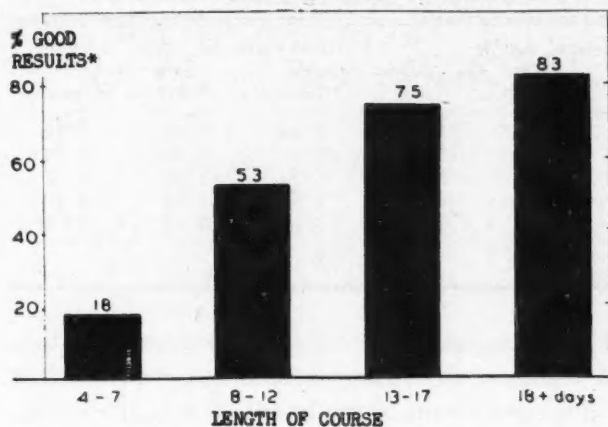
In the children who were oedematous before treatment, 68% of the courses resulted in loss of oedema. If the courses shorter than 8 days are excluded (Fig. 1) 74% of courses resulted in loss of oedema. In the 34 courses given to children who were free of oedema 74% resulted in loss of proteinuria.

In children who were given more than one course of hormone, the results from the later courses were not quite as good as for the first, averaging 65% good results (i.e. loss of oedema or proteinuria or both) as compared with 73%, but of the four children who had 6 courses, three had a good result from the 6th course.

In the entire series of 88 children, 70 (80%) had a good result from at least one course of hormone, and the remaining 20% failed to react favourably to one or more courses.

ACTH and Cortisone Therapy of Nephrotic Syndrome in Children

Effect of Length of Course on Results



*LOSS OF OEDEMA OR PROTEINURIA OR BOTH
Fig. 1

2. Effect of length of course on result

This is shown graphically in Fig. 1. Courses of less than eight days' duration were almost useless and the best results were obtained when treatment continued for more than 12 days.

3. Biochemical effects

The improvement in serum protein and cholesterol values is shown in Table II. It may be noted that the biochemical changes at the commencement of treatment varied with the severity of the disease. Thus, in groups 4 and 5, in which there was no oedema before therapy, the serum cholesterol was lower and the serum protein higher than in the oedematous children. It was found that the better the clinical result, the closer to normal were the serum cholesterol and protein values after treatment.

The rise in total serum protein is seen to be due almost entirely to a rise in the albumin fraction. We have observed that the "critical" level of serum albumin is about 1.0 g. %, most children with a lower level being oedematous, and with a higher level being free of oedema.

Maintenance Hormone Therapy

Very soon after it was found that ACTH and cortisone might produce a remission of the disease, it was learned that unfortunately such remissions were seldom permanent, and that oedema might return immediately, or weeks or months later. Our longest remission followed by a recurrence is in a boy who was free of oedema and proteinuria for three years and eight months,

when an exacerbation occurred after an infection. (However, in some children there has been no recurrence and they are apparently well more than two years later. Nine of 53 children treated before June 1952, are still well 2½-4 years after therapy.)

The next logical step was to give hormone over a prolonged period after the initial course. When only short-acting ACTH was available it was not practical to give frequent injections at home, but cortisone could be given by mouth and we then tried giving daily doses of cortisone at home following hormone-induced remission.

The first seven children so treated were given small doses of cortisone, 10-25 mg. daily. Four of them had longer remissions than they had had after earlier courses of ACTH, and one is still well. (He was given 12.5 mg. cortisone daily for 16 months, and it was stopped 9 months ago.) The other three children had a recurrence of the disease after a few weeks.

It was at this time that Lange's first report appeared on the use of high doses of cortisone given intermittently.⁶ His reasoning, based on serum complement studies, was that the hormones depress antibody production and so stop the antigen-antibody reaction which is damaging the kidney. By following serum complement levels, he found that they rose before diuresis occurred and fell before an exacerbation. He gave 400 mg. cortisone daily for three consecutive days a week and found that serum complement remained normal and remissions continued. In a recent paper⁷ he reported that this method had been successful in 16 of 18 patients who received intermittent cortisone for 6-30 weeks after an ACTH-induced remission. One patient died from a septic condition, but apart from this he reports no serious side-effects.

We had felt it would be better to start with smaller doses, increasing them gradually as necessary, largely because we had been impressed by the serious complications which may occur under continuous hormone therapy. We hoped that for each child a dosage schedule might be found which would be sufficient to maintain the remission but not so high as to cause complications. We have started maintenance therapy with cortisone at 75-150 mg. per day for three consecutive days a week. Sixteen children have been treated this way for periods up to one year. Eight are still free of oedema and proteinuria, 3-14 months after starting

TABLE II.

ACTH AND CORTISONE THERAPY OF NEPHROTIC SYNDROME IN CHILDREN. CHANGES IN SERUM CHOLESTEROL AND PROTEINS RESULTING FROM THERAPY.								
Group	Clinical classification of patients		Serum cholesterol, mg. %		Serum protein, g. %			
	Before therapy	After therapy	Before therapy	After therapy	Before therapy Total	After therapy Albumin	After therapy Total	After therapy Albumin
1	Edematous	Ed-free, Prot-free*	565	285	3.82	0.85	5.67	2.74
2	Edematous	Ed-free	613	340	3.75	0.75	5.40	2.22
3	Edematous	Unchanged	666	527	3.72	1.03	3.80	1.07
4	Ed-free	Prot-free	433	310	5.19	1.91	6.12	3.20
5	Ed-free	Unchanged	414	366	5.06	1.66	5.19	2.14

*See footnote to Table I.

maintenance cortisone. The other eight had recurrences in from one week to four months, and four have since improved on a higher dosage. One child died suddenly and unexpectedly. She was a 2-year-old girl in whom the disease had been present for three months. She had lost her oedema during a course of ACTH and was sent home on 75 mg. cortisone a day for three consecutive days a week. After the fourth week she developed abdominal pain and vomiting, was brought back to hospital, and suddenly died while sitting up on the examining table. Post-mortem examination showed no cause for death, though some cerebral and pulmonary oedema was present.

In summary, our present plan of hormone therapy is to give ACTH in hospital early in the disease to produce a remission, then to give intermittent cortisone at home for several months in the hope of preventing a return of the disease.

Although this method seems successful in many children, and there is hope that with greater experience better dosage schedules may be worked out, our optimism must remain guarded for the following reasons:

1. Some children never respond to the hormones and progress relentlessly to renal destruction, uræmia and death.

2. Rarely a child may die as a result of hormone treatment, from known or unknown cause, either during the initial course or during maintenance therapy.

3. A nephrotic child may still die of uncontrolled infection.

4. Some danger may result from the prolonged suppression of adrenal cortical activity by cortisone.

As far as the effects of such hormone therapy on the child's chances for ultimate cure are concerned, we cannot draw any conclusions for some years yet, until we know that children so

treated are still well after 3 or 4 years, and that a significantly higher percentage recover than with other forms of treatment. This is presented, then, not as the final form of treatment for a child with the nephrotic syndrome, but rather as the current stage reached in working toward the ultimate ideal, the cure of the disease.

SUMMARY

1. The clinical course of the nephrotic syndrome in children has been briefly presented.

2. Symptomatic treatment of the disease is outlined, with emphasis on treatment of infections and relief of oedema.

3. Infusions of 6% salt-free dextran were given to six children with variable results.

4. Our experience in treating 88 nephrotic children with ACTH and cortisone is described. Seventy-four per cent of oedematous children lost their oedema, and when non-oedematous children with proteinuria were treated, 74% showed clearing of the urine.

5. Poor results were obtained when hormone treatment was given for less than eight days, and the best results followed courses of 12 days or longer.

6. Maintenance treatment with intermittent cortisone is now being tried in the hope of prolonging remissions, and our results in 16 children are briefly described.

REFERENCES

1. BARNETT, H. L., FORMAN, C. W. AND LAUSON, H. D.: The Nephrotic Syndrome in Children. In *Advances in Pediatrics*, Levine, S.Z., ed., The Year Book Publishers, Inc., Chicago, 1952, Vol. 5, p. 53.
2. BARNES, L. A., MOLL, G. H. AND JANEWAY, C. A.: *Pediatrics*, 5: 486, 1950.
3. EIBEN, R. M., KLEINERMAN, J. AND CLINE, J. C.: *J. Pediat.*, 44: 195, 1954.
4. KELLEY, V. C. AND PANOS, T. C.: *J. Pediat.*, 41: 505, 1952.
5. WALLENIUS, G.: *Scandinav. J. Clin. & Lab. Invest.*, 2: 228, 1950.
6. LANGE, K., SLOBODY, L. AND STRANG, R. H.: *A. M. A. Am. J. Dis. Child.*, 86: 478, 1953.
7. *Idem*: *Pediatrics*, 15: 156, 1955.

Case Reports

THE TREATMENT OF ACUTE FULMINANT HEPATITIS WITH CORTICOTROPIN AND CORTISONE*

S. J. SHANE, M.D., F.R.C.P.[C.], F.A.C.P., F.C.C.P.,
A. R. GAUM, M.D., F.A.C.S., F.I.C.S., and
DAVID GAUM, M.D., C.M., Sydney, N.S.

SINCE THEIR INTRODUCTION as therapeutic agents, corticotropin and cortisone have been utilized in many diseases of diverse etiology, sometimes with a rational basis and sometimes without. In general, it may be stated that new uses for these hormones have been found either by analogy with diseases in which they have been effective, or in cases in which they have been used as a last resort when all other therapeutic measures have failed. It was therefore natural to attempt to determine their effect in hepatic disease, whether chronic, acute or fulminant. As early as 1950, Webster¹ reported his experiences in nine cases of various forms of acute and subacute liver disease with "extract of adrenal cortex." All nine patients recovered promptly and laboratory tests rapidly reverted to normal after treatment. Re-examination after a year revealed no evidence of liver dysfunction, even in those with a history of chronic liver disease. In 1951, Colbert and others² described their results in five cases of acute viral hepatitis, given 100 mg. of ACTH daily for periods of 9-21 days. They reported that marked symptomatic improvement occurred promptly and was associated in all instances with a falling serum bilirubin concentration. There has been some difference of opinion, however, as to the value of corticotropin and adrenal cortical steroids in portal cirrhosis. Helm³ reported satisfactory results in a 53-year-old woman with Laennec's cirrhosis, who was in critical condition when first seen, and made a highly satisfactory recovery, apparently as the result of cortisone therapy. On the other hand, in a study of 10 patients with advanced portal cirrhosis, Sklar and Young⁴ were unable to discern any significant benefit from the use of corticotropin and corticoids in high dosage. Some of these patients were in hepatic coma or pre-

coma, while others showed evidence of liver failure without coma. All these patients died, and none showed even transitory benefit. An unexpected observation in this study was the failure of treatment to produce even the usual non-specific effects on mood and appetite. It is distinctly possible that, when hepatic failure supervenes in a patient with advanced chronic liver disease, even such potent therapeutic agents as these may be of no value. However, it appears likely that, in acute hepatic disease, even when it has progressed to the stage of hepatic failure, the pathological changes may be reversible, and recovery may be brought about by the use of these hormones. As is usually the case, careful and controlled studies have somewhat limited the enthusiasm with which these therapeutic agents were originally greeted in the treatment of liver disease. A series of such studies by Evans and others⁵⁻⁷ appeared to indicate that corticotropin is of very little value in acute and chronic hepatic disease, that cortisone may be of some value in acute disease but not in fulminant cases, and that these hormones may leave patients more vulnerable to relapses. Nevertheless, when large numbers of patients with infectious hepatitis were subsequently treated with cortisone, using adequate controls,⁸ this form of treatment was found to be of distinct value. The results of this particular study indicated that cortisone causes a more rapid clearing of jaundice than occurs in controls, that laboratory findings tend to return to normal faster, and that such patients on cortisone therapy regain their appetite sooner, eat more food and gain more weight than is the case in controls. The data in this study also indicate that cortisone-treated patients become well sooner and do not require treatment so long. It would therefore appear that patients who do not respond to the usual supportive measures, or whose recovery with such measures is in doubt, should certainly be given a trial on corticotropin or cortisone or both.

The case reported below is one of acute fulminant hepatitis in which the onset of hepatic coma was suspected, and in which dramatic improvement and eventual complete recovery resulted from the use of both these hormones.

Mrs. S.A., 58 years of age, was admitted to the City of Sydney Hospital on January 13, 1955, complaining of jaundice. Her previous history was not contributory. She had been previously attended by one of us (A.R.G.) for "nervousness", and on the day of admission had called this physician, complaining of jaundice. She was imme-

*From The City of Sydney Hospital, Sydney, N.S.

diately transferred to hospital, where physical examination was completely negative with the exception of rather deep icterus and a large tender liver, felt four fingerbreadths below the right costal margin. A clinical diagnosis of infectious hepatitis had been made, and the patient was placed on a high protein, high carbohydrate, low fat diet. Examination of the blood revealed a haemoglobin value of 13.7 g. per 100 c.c., a red cell count of 4,980,000 and a white cell count of 7,300 per c.mm. The differential count was within normal limits. The blood sugar was 101 mg. per 100 c.c., the blood urea was 28 mg. per 100 c.c. and the urea nitrogen was 13 mg. The icterus index was 90. The blood group was found to be O, Rh positive. The serum bilirubin was 20 mg. per 100 c.c. The prothrombin concentration was 50% of normal. Urinalysis revealed a specific gravity of 1.019, a trace of albumin, a 4+ reaction for sugar (patient had been receiving intravenous glucose), a trace of acetone and a 4+ test for bile. Microscopic examination revealed a few white blood cells and an occasional red blood cell. Examination of the stool for occult blood gave a 4+ test. The cephalin flocculation test was 4+ on two occasions.

For the next 48 hours, the patient's condition progressively deteriorated, and one of us (S.J.S.) was called in consultation on January 15. At that time, the physical findings were essentially the same as had been the case 48 hours earlier, but, at this time, signs of impending hepatic coma were noted, in that the patient was semi-stuporous, difficult to arouse, and irrational when it was possible to gain her attention. In addition, the liver edge was now five fingerbreadths below the costal margin, there was evidence of ascites, and there were large ecchymoses scattered over the entire body surface. Vaginal bleeding was also noted.

The diagnosis of infectious hepatitis was concurred in, but it was felt that we were dealing with either a fulminant case of this disease or with an acute hepatic necrosis, presumably of viral origin. After prolonged discussion, it was decided to continue with supportive measures, but that, if no improvement was evident within 24 hours, corticotropin should be considered. On the following day no improvement was noted, and corticotropin was started in a dosage of 40 mg. intravenously every eight hours in 500 c.c. normal saline. In addition, aureomycin was administered in a dosage of 250 mg. every four hours, blood transfusions were begun, and synthetic vitamin K was given in 50 mg. doses daily.

Over the next 72 hours, there was gradual and continued improvement in the patient's condition, and she was seen again in consultation (S.J.S.) on January 20, 1955. At that time her general condition appeared dramatically improved as compared with that on January 15. Her sensorium was far less clouded, and the liver was distinctly smaller, being now three fingerbreadths below the right costal margin. This latter finding was not necessarily considered a sign of improvement. However, whereas there had previously been a degree of oedema of the extremities, this was now no longer present. The pulse was 80 per minute, and of good quality. The blood pressure was 130/80 mm. Hg. At this point, it was felt that striking improvement had taken place, but the final outcome was still in doubt.

The dose of corticotropin was gradually decreased, and hydrocortisone was begun in doses of 200 mg. daily, in such a manner that for a period of 2½ days the patient was receiving both corticotropin and hydrocortisone. The patient was continued on a high protein, high carbohydrate diet, with supplementary potassium chloride in doses of 6.0 g. daily. The transfusions and the vitamin K were also continued. During the next few days, the laboratory findings gradually returned to normal as the clinical condition improved, although the cephalin flocculation test remained abnormal. The remainder of the patient's course was uneventful, and she was discharged to her home, without jaundice and clinically well, on February 24, 1955.

DISCUSSION

There seems to be little doubt that this patient was in, or entering, the state of hepatic coma, when she was seen on January 15; and it seems difficult to attribute her dramatic recovery to any medication other than the corticotropin and cortisone. There is a distinct possibility, however, that the use of aureomycin may have influenced the satisfactory outcome. Farquhar and others⁹ reported four cases of acute hepatic coma, all of which recovered following aureomycin therapy, and they attributed the satisfactory result to the use of aureomycin. We have, however, been unable to corroborate this finding by a rather extensive search of the literature, and the weight of evidence seems to be in favour of the hormones as the major agents in bringing about recovery in this case. It might have been wiser and more scientific to use one agent or the other (i.e. either aureomycin or hormones); but the patient's condition was felt to be so precarious that it was considered unwise to temporize. Moreover, in certain circles, it is always considered desirable to use a broad-spectrum antibiotic in all seriously ill patients in which large doses of corticotropin or cortisone or both are being given.

It would seem reasonable, therefore, to consider the use of corticotropin or cortisone or both in patients seriously ill with infectious hepatitis who are not responding to the usual supportive measures. It would also seem wise in such cases to combine a broad-spectrum antibiotic, preferably aureomycin, with the hormonal therapy. We do not, however, advocate hormonal therapy in all cases of infectious hepatitis since, in our experience, most of these patients recover satisfactorily without specific treatment.

SUMMARY

1. A case of acute fulminant infectious hepatitis with hepatic coma is reported, in which dramatic improvement and final recovery followed the use of corticotropin and cortisone.

2. It is possible that the patient's recovery was influenced by concomitant treatment with aureomycin; but the weight of evidence is in favour of the hormones as the major agents in bringing about recovery.

3. It is recommended that corticotropin or cortisone or both be used in cases of severe infectious hepatitis which do not respond to supportive measures.

4. The recent literature on this subject is reviewed.

REFERENCES

1. WEBSTER, J. J.: *Ann. Int. Med.*, **33**: 854, 1950.
2. COLBERT, J. W., JR. *et al.*: *New England J. Med.*, **245**: 172, 1951.
3. HELM, S.: *J. A. M. A.*, **151**: 382, 1953.
4. SKLAR, M. AND YOUNG, I. I.: *Am. J. M. Sc.*, **229**: 138, 1955.
5. EVANS, A. S., SPRINZ, H. AND NELSON, R. S.: *Ann. Int. Med.*, **38**: 1115, 1953.
6. *Idem*: *Ibid.*, **38**: 1134, 1953.
7. *Idem*: *Ibid.*, **38**: 1148, 1953.
8. HUBER, T. E. AND WILEY, A. T.: *Ibid.*, **42**: 1011, 1955.
9. FARQUHAR, J. D. *et al.*: *Am. J. M. Sc.*, **220**: 166, 1950.

HEPATO-LENTICULAR DEGENERATION

L. R. COKE, M.D., F.C.C.P., F.A.C.P. and
E. G. SHAW, M.D., Winnipeg, Man.

IT IS USUAL for some degree of liver damage to be present in chronic heart disease. In advising management for the heart the requirements of the liver should be considered, and its further injury by such factors as over-digitalization, anoxia and alcoholism should be avoided if possible. The following case is reported because lenticular degeneration was found at autopsy in a man who had suffered from chronic heart disease, from liver infections, and also from the causes of liver damage mentioned above.

A 32-year-old veteran of World War II, with no family history of liver disease or of other relevant illness, fell sick at the age of 20 years with malaria. He was serving in Italy at the time, and on being evacuated to a hospital in North Africa he was also discovered to have mitral stenosis in spite of a negative history of rheumatic infection or of heart trouble.

He recovered from the malaria and returned to duty, but two years later, just before being discharged from the Army, he had an attack of infectious hepatitis. This illness took an uneventful course and again he recovered, but subsequently he was repeatedly admitted to D.V.A. hospitals with complaints of precordial pain, dyspnoea, fatigue, hæmoptysis and joint pains. At this time he was going from one job to another; he was drinking heavily and was estranged from his wife. Because he seemed to be using the hospitals as emotional sanctuaries, he was labelled in 1948 as an inadequate personality and in this assessment his war service seems to have been overlooked.

In 1952, when he was 30 years old, he developed acute pulmonary oedema and while he was in hospital he was found to have subacute bacterial endocarditis. He was regarded as a difficult patient, being unstable, immature and poorly disciplined, and he was now diagnosed as a psychopathic personality. A second admission to hospital was necessary in 1952, when he was suffering from the effects of several arterial emboli. He also had considerable anorexia, nausea and vomiting.

He lost much weight. In 1953 he was admitted on three occasions for the control of various degrees of congestive heart failure precipitated by his omission to take digitalis because of his whim or of his alcoholic bouts. Sometimes his liver was noticed to be enlarged, and on a fourth admission in that year, liver function tests indicated functional insufficiency; the bromsulphalein retention was 22% in an hour, the thymol turbidity was 3 units, the thymol flocculation +++, and the cephalin flocculation ++. A blood sugar level at this time was 50 mg. %. On this admission, besides the deterioration in his personality which had already been recorded by the change in diagnosis from inadequacy in 1948 to psychopathy in 1952, definite neurological signs were made out. These were a tonus increase and a comparative immobility of the left arm, but the tendon jerks remained unaltered and the patient was capable of moving the arm when his attention was distracted.

In January 1954, a mitral valvulotomy was performed. He did well for four days after the operation, but unfortunately bacterial endocarditis supervened and he went downhill in spite of intensive antibiotic therapy. An electrocardiogram in February 1954 revealed digitalis overdosage. He refused food and fluids; his hæmoglobin level fell 45%; he became jaundiced and comatose. Glutamic acid brought about a temporary improvement, but he died in March 1954.

At autopsy the right lenticular nucleus was found to be softened and microscopic section showed a liquefaction necrosis without inflammatory reaction (Fig. 1). The rest of the brain was normal. The liver was granular and on section showed interspersed hæmorrhagic and pale areas. It weighed 1,990 g. Microscopically the appearances were those of subacute yellow atrophy, with congestion, marked parenchymatous degeneration, and a moderate increase in the fibrous trabeculae (Fig. 2). The heart weighed 450 g.; a fibrinous pericarditis was present and the mitral valve was calcified and extremely narrow.

The copper content of the liver was found to be 0.50 µg. per g., a total of 100 mg. copper. This is less than the normal.

DISCUSSION

When Wilson described the syndrome of hepato-lenticular degeneration, he said that he thought the hepatic disorder preceded the cerebral damage, and since that time evidence has accumulated that in both man and animals degeneration of the basal ganglia is liable to occur as a result of severe and long-standing liver damage.^{1, 5, 9, 10, 16, 18} In the case described here, there were several factors which can reasonably be implicated in the production of such damage. The insults to the integrity of the liver included malaria and infectious hepatitis; malnutrition, anoxia, hypoglycæmia; and over-digitalization. There were also at work the effects of the mitral lesion. Liver function tests become abnormal in rheumatic heart disease¹¹ and also in heart failure. The development of central lobular necrosis resulting from anoxia and hepatic congestion to diffuse hepatic fibrosis has been traced by means of serial biopsies and by necropsy examination.¹⁵ Paul White has drawn attention to the atrophic and regenerative areas which occur after years of venous congestion,

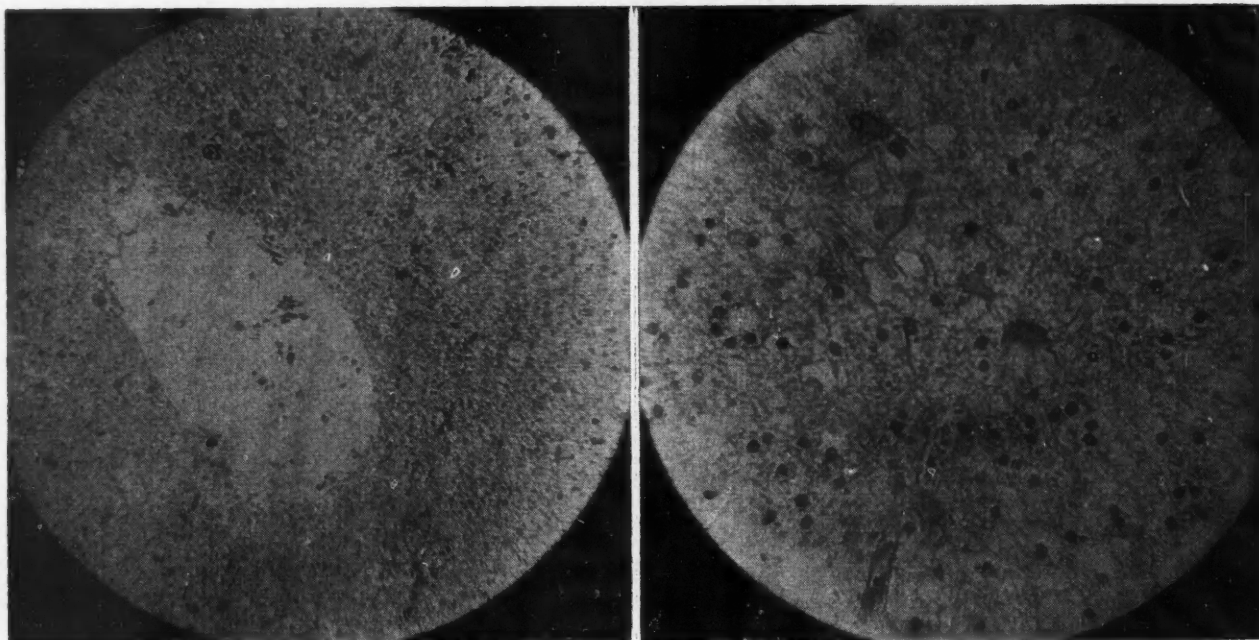


Fig. 1.—Section of right lenticular nucleus.

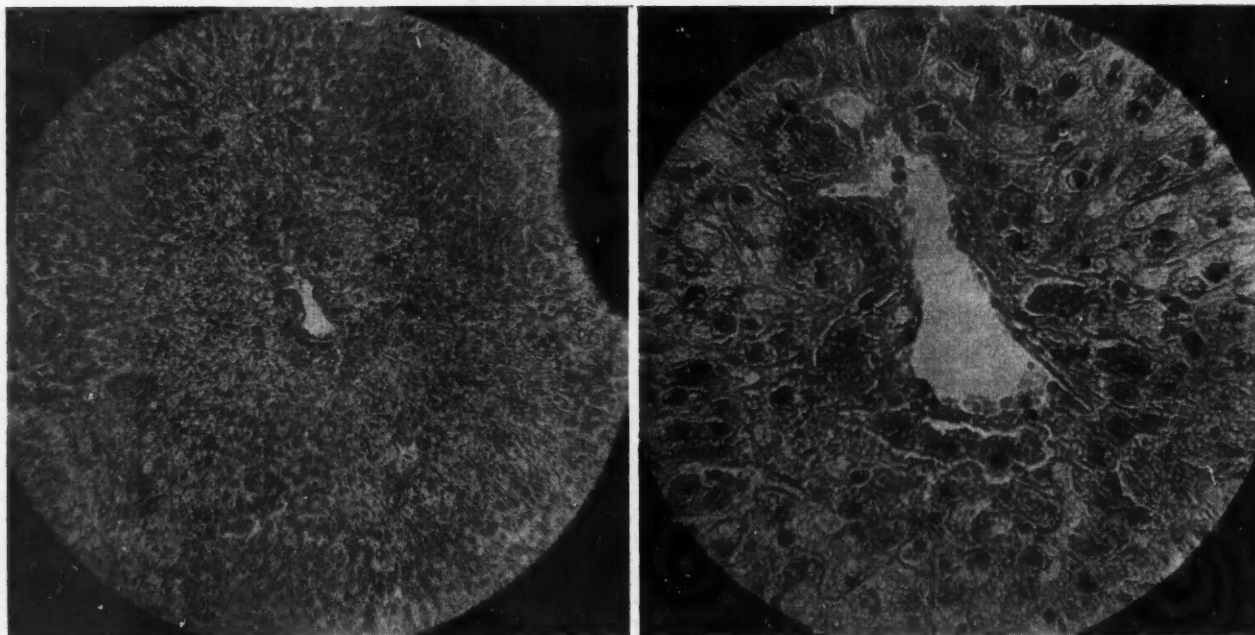


Fig. 2.—Section of liver.

and to the fact that finally a real cirrhosis may become established. Malnutrition may further stimulate these cirrhotic tendencies.¹⁹

It was Glazebrook⁶ who first suggested copper as the connecting link between liver disease and lenticular degeneration and put forward the idea that this heavy metal, which poisons respiratory enzymes, accumulates because the damaged liver is unable to secrete it and affects the tissues which lie in the basal ganglia and the cerebral cortex because they have the fastest respiratory rates of any in the body. While the metabolism

of copper is clearly disturbed in the hereditary disease where copper excess is found in the urine, the liver, the lenticular nucleus and the Kayser-Fleischer rings, the acquired cases of hepato-lenticular degeneration do not generally show these abnormalities. Copper is normally excreted in the bile,¹⁵ and whether or not it is dammed back in the body depends on the type of liver lesion; thus biliary cirrhosis² plays a major role in copper retention, while portal cirrhosis without significant biliary obstruction does not affect copper levels appreciably. The liver copper

content in our case was lower than normal, but the noxious influences acting upon the liver were those liable to produce a portal rather than a biliary cirrhosis; high values therefore were not to be expected and it seems improbable that copper poisoning of respiratory enzymes was responsible for the lenticular lesion. But there were other possibilities; anoxia and hypoglycæmia in the brain have frequently been observed, and Lawrence¹² found that the putamen, caudate nucleus, and cerebral cortex were most affected by hypoglycæmia. The cerebral effects of digitalis were well known to Withering and were later emphasized by Mackenzie.¹³ Hueper⁸ described the parenchymatous cerebral lesions of digitalis poisoning as "foci of vacuolated and disintegrating ganglion cells, necroses, and glia cell proliferation. The basal ganglia and the cerebellum were the sites of these manifestations"

Recently it has been postulated that the fundamental defect in Wilson's disease is an increased absorption of copper by the intestine, which is then laid down in excess in the affected tissues.² There was no evidence of such a functional disorder being present in our case although it may be operative in a selective group; it would seem that Wilson's disease, with its definite but as yet unexplained disturbance of copper metabolism, is only one of several conditions which make up the hepato-lenticular syndrome.^{2, 7}

In the first stages of Wilson's disease, neurotic or psychiatric symptoms may colour the picture and lead to the patient's being admitted to a mental hospital. This did not happen to our man, but his deterioration of personality was observed long before the physical signs of immobility and tonal increase in the left arm appeared, and this deterioration did not receive sympathy but raised the suspicions that he was using the hospitals as emotional sanctuaries.

SUMMARY

1. Lenticular degeneration was found at autopsy in a man suffering from mitral stenosis.
2. Although liver disease was also present and was probably of long standing, other non-hepatic features may have contributed to the lenticular damage.
3. "Wilson's disease" is only one of several conditions which make up the hepato-lenticular syndrome.

We wish to thank Dr. A. J. Glazebrook for his assistance.

REFERENCES

1. ALEXANDER, L.: *Proc. A. Res. Nerv. & Ment. Dis.*, 21: 334, 1942.
2. BALTZAN, D. M.: *Canad. M. A. J.*, 34: 544, 1936.
3. BEARN, A. C. AND KUNKEL, H. G.: *J. Clin. Invest.*, 33: 400, 1954.
4. COKE, L. R.: *Manitoba Med. Rev.*, 27: 422, 1947.
5. DOBBERSTEIN, J. J.: *Handbuch der speziellen pathologischen Anatomie der Haustiere*, R. Schoetz, Berlin, 1926. Vol. 2, p. 594.
6. GLAZEBROOK, A. J.: *Edinburgh M. J.*, 52: 83, 1945.
7. GREENFIELD, J. G.: *Proc. Roy. Soc. Med.*, 47: 150, 1954.
8. HUEPER, W. C.: *New York J. Med.*, 45: 1442, 1945.
9. HUTYRA, F., MAREK, J. AND MANNINGER, R.: *Special pathology and therapeutics of disease of domestic animals*, Baillière, Tindall and Cox, London, 1938. Vol. 2, p. 3881.
10. KALKUS, J. W., TRIPPER, H. A. AND FULLER, J. R.: *J. Am. Vet. M. A.*, 68: 285, 1925.
11. KISSANE, R. W. *et al.*: *Am. J. M. Sc.*, 219: 48, 1950.
12. LAWRENCE, R. D., MEYER, A. AND NEVIN, S.: *Quart. J. Med.*, 11: 181, 1942.
13. MACKENZIE, J.: *Heart*, 2: 273, 1911.
14. MOSCHOWITZ, E.: *Ann. Int. Med.*, 36: 933, 1952.
15. SHERLOCK, S.: *Brit. Heart J.*, 13: 273, 1951.
16. STADLER, H.: *Ztschr. f.d. ges. Neurol. u. Psych.*, 154: 626, 1935.
17. VAN RAVESTEYEN, A. H.: *Acta med scandinav.*, 118: 163, 1944.
18. WAGGONER, R. W. AND MALAMUD, N.: *J. Nerv. & Ment. Dis.*, 96: 410, 1942.
19. WHITE, P. D.: *Heart disease*, 4th ed., The Macmillan Company, New York, 1951. p. 168.
20. WILSON, S. A. K.: *Brain*, 34: 295, 1912.

Special Article

A CHILD GUIDANCE CLINIC FOR SCHOOL CHILDREN

J. L. ASSELSTINE, M.D., Winnipeg

THE CHILD Guidance Clinic of Greater Winnipeg was organized in May 1951, to operate under the joint auspices of the Province of Manitoba through the Psychiatric Services of the Provincial Department of Health and Public Welfare, and the School Board of Winnipeg School District No. 1. The new agency, an expansion of the clinic organized by the Winnipeg School District in 1941 to serve city schools, was designed to provide a child guidance service to children attending school in the immediately adjacent suburban municipalities as well as Winnipeg proper.

ADMINISTRATION

The director, who is a qualified psychiatrist, is jointly responsible to the Provincial Psychiatrist and the Superintendent of Winnipeg School District No. 1 for the operation of the clinic (see Fig. 1). The professional staff of 28*

*All statistics quoted in this article are from the clinic annual report for the operational year September 1954 to June 1955.

and clerical staff of four, with the exception of the director, who is a Provincial Civil Servant, are engaged through the agency of the Winnipeg School District. Of the total staff of 32, the School District recovers the salaries of 12 from Federal Mental Health Grant funds administered by the Province. This latter group represents the additional staff provided for when the present organization was instituted in 1951. The equivalent of their time is available to both

est in the application of mental health principles would be difficult to achieve without an active treatment and follow-up programme for the more disturbed children who may be of concern to the teacher. Clinic facilities are utilized by the Faculty of Medicine for both graduate and undergraduate training. Students from the School of Social Work are attached to the visiting teacher department for field work and block placement.

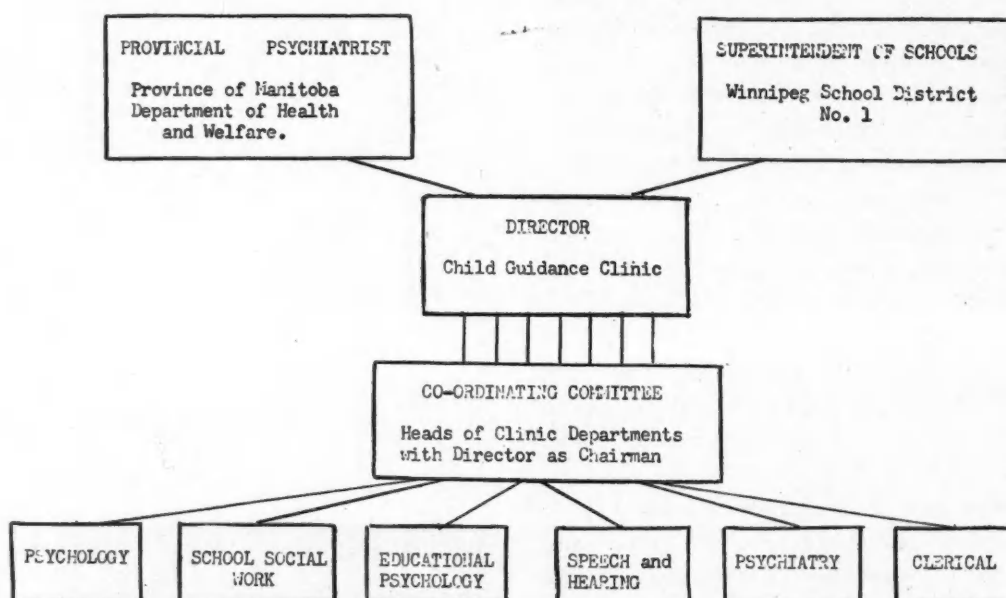


Fig. 1.—Administrative set-up of the Child Guidance Clinic of Greater Winnipeg.

city and suburban areas, roughly in proportion to the relative populations involved.

ORGANIZATION AND FUNCTION

The clinic is organized in six departments: psychology, visiting teacher (school social work), reading (educational psychology), speech and hearing, psychiatry, and clerical. Each department has a head who is responsible for his or her own programme. Matters involving more than one department, or the clinic as a whole, are decided at weekly meetings of a co-ordinating committee composed of the heads of departments and chaired by the director. The relationship of the clinic to outside agencies is the responsibility of the director.

The functions of the clinic may be listed as case-finding and diagnosis, treatment and follow-up, consultation, training and education, study and research. The preventive work of the clinic centres round the close association with the schools which makes possible contacts with teachers and administration, or through brief individual service to child and parent with subsequent interpretation to school staff. Support for clinic facilities and the maintenance of inter-

REFERRALS

Any of 58,000 children attending a public, parochial or private school in the area covered are eligible for referral. No individual charges of any kind are made for services given. In all departments, at least one-third of the children seen are referred by school personnel. The bulk of the remainder are from parents, physicians and community agencies, the proportion varying from one department to another. Of the 4,200 children who received attention last year through the combined clinic services, 100 had a full study including a psychiatric examination. The Central Reference Index now registers the names of 19,000 children referred since 1943, who have had diagnostic and follow-up attention in at least one department.

In general, reasons for referral to the clinic can be grouped as personality problems, situational problems, reaction problems, intellect variations or organic problems. A child may have difficulties in any or all of these categories. Usually one predominates and characterizes the clinical picture. In addition, specific types of problems such as academic retardation and speech defects are the responsibility of individual departments.

DEPARTMENTS

The psychology department, with a staff of seven, administered 1,336 individual intelligence tests last year. Almost all of these tests were administered in the school attended by the child. The teacher and the principal are interviewed for background material and interpretation both before and after the testing. Frequently during these interviews, the teacher wishes to discuss other children in her class about whom she is concerned. For some of these a clinic referral is recommended before advice can be given. The frequency distribution of the intelligence quotients of children tested very closely follows the normal curve found in the general population. Other functions of the department include vocational guidance, personality analyses, play therapy for cases having a full clinic study, and specialized testing for the mentally and physically handicapped.

Ten school social workers are employed in the visiting teacher department. Two are engaged full time in intensive case work as members of the psychiatric therapy team. They visit the schools as necessary to report to the teacher involved on cases being carried. A full interpretation is given in order to enlist to the fullest possible extent the teacher's understanding co-operation in the treatment programme. The remaining workers visit frequently in the schools and home. The majority of their cases are brief contacts although individual workers, depending on their training and experience, carry a varying load of longer-term case work. Of the 2,760 referrals accepted last year, 191 had intensive service.

The reading department, with four educational psychologists, made a complete academic diagnosis of 163 children last year, including 13 who had a full clinic study. Tutoring of 57 children, individually or in small groups, was carried out. Not less than 80% of the children who came to psychiatric study in this clinic are academically retarded although of average or above-average intelligence. Tutoring by a reading clinician acting as a member of the psychiatric team may be recommended at the diagnostic case conference as the treatment of choice for the child. The methods used vary from formal tutoring with specialized or alternate teaching materials, to modified play interviews with a minimum of direct attention to school work.

The speech and hearing department locates cases of speech and hearing defect through school surveys, as well as accepting individual referrals. When a school is surveyed, each child has an individual "sweep check" on a pure-tone audiometer and a short speech test. The methods used reveal that about 4% of the children tested have a hearing defect of minor or major degree, and that about 10% have a speech problem. Following the necessary diagnostic procedures

in the cases screened out, a corrective programme is set up in the school. The effectiveness of the treatment is the result of the co-operation of the parents, teachers, speech therapists, school nurses and physicians. The staff of six therapists last year surveyed 2,542 students in five schools; 396 cases were treated individually or in small groups, and 80 children were carried as "classroom cases" by the teacher under the therapist's supervision.

The director is able to devote about half of his time to psychiatric examinations and treatment. Additional service to a maximum of one-half day weekly is given by the staff of the Provincial Psychopathic Hospital. Because of the limitations in psychiatric time available, only 100 children had a full clinic study including a psychiatric examination last year, and only two were given intensive therapy by a psychiatrist. Immediate expansion of these services is limited not only by personnel but also by physical facilities available. All referrals for study are carefully screened at an intake conference. No long-term waiting list is accumulated. Cases which cannot be scheduled in the near future are offered such service as can be given through other departments of the clinic with or without the additional help of other community facilities, both private and public.

The clerical department is composed of the clinic secretary and three stenographers. Their duties are organized to relieve other personnel of all routine work not requiring professional training. The secretary receives all referrals made directly to the clinic. Requests for a specific type of service are transmitted to the head of the department concerned who further screens them as required. General requests are transmitted to the social work department. The same department also receives the psychiatric referrals in order that sufficient information may be gathered for intake conference. From her knowledge of all community facilities, the secretary is able to guide persons seeking a service not provided by the clinic.

SUMMARY

The organization and function of a child guidance clinic, operated jointly by a provincial government and a city school board to provide a comprehensive service for the school children of a metropolitan area, is described. Relevant statistics for the year 1954-55 are given.

Child Guidance Clinic of Greater Winnipeg,
Ellen and Bannatyne Sts.,
Winnipeg 2.

Clinical and Laboratory Notes

A NEW TECHNIQUE FOR THE LOCAL USE OF HYDROCORTISONE IN RHEUMATIC DISEASE*

A. W. BAGNALL, M.D., M.R.C.P.(Lond.),
F.R.C.P.[C.], Vancouver, B.C.

IN 1950, THE AUTHOR made rather extensive studies of the value of cortisone injected into joint cavities. The results, as in previous trials of procaine and of lactic acid, were most disappointing.

In 1951, through the kindness of Merck & Co. Limited, hydrocortisone acetate was made available and experience with its use by local injection was much more satisfactory. However, in the course of some 6,000 regional injections in the intervening four years, modification in the technique of using hydrocortisone by local injection proved to be necessary in about 25% of cases.

A review late in 1951 of the use of local hydrocortisone, at that time being given only by injection into joint cavities, showed an unexpectedly high incidence of unsatisfactory results. Although it was realized that no therapeutic agent could bring about uniformly perfect results, the good results were nevertheless so good that careful analysis of the failures seemed indicated. There was no explanation for some of these failures, but when consideration was given to possible anatomical variations in the site of inflammation, it was realized that failure of hydrocortisone by local injection might sometimes be explained by failure to bring it into contact with the inflamed tissues giving rise to the joint pain because they, in turn, were not in contact with the joint cavity. Thus, while synovitis of the knee might respond favourably to injection of hydrocortisone into the joint cavity, subacromial bursitis could hardly be expected to respond to injection into the shoulder-joint itself, because the latter practically never communicates with the subacromial bursa.

TECHNIQUE OF DIFFERENTIAL DIAGNOSTIC INJECTION

Localization of the precise source of pain in or around a joint is very difficult, both for patient and physician. To carry out a satisfactory

injection in *problem cases*, it was necessary to find some "indicator" to ensure that the hydrocortisone had been brought into contact with the inflamed tissue.

Tenderness on palpation, and/or pain on passive manipulation, are characteristic signs of inflammation in or around a joint. It was therefore decided to use, as an *indicator*, a local anaesthetic (procaine) blended intimately with the hydrocortisone. The criterion of a satisfactory injection was that local tenderness, as well as pain on passive or active manipulation, must be neutralized almost completely at the end of the injection.

In practice, it has been found that when pain is elicited in soft tissue at the point of the needle, it usually indicates an inflammatory focus and therefore an indication for infiltration of the hydrocortisone-procaine mixture into that spot. Also, if a significant proportion of the tenderness, or of the pain on manipulation, remains at the end of such an injection, the results are correspondingly poor because the hydrocortisone has not been injected into the proper location. In the mixture, the procaine "indicator" accomplishes temporarily, in a very few minutes, the more lasting results to be hoped for in the next few days from the hydrocortisone. Differential anatomical diagnosis of the actual source of pain, whether actually in the joint or around it, is thereby accomplished.

An adverse painful reaction is occasionally encountered when pure hydrocortisone is injected directly into a joint cavity. This is encountered more often when hydrocortisone-procaine mixtures are used, but the increased pain in the 12-24 hours after the injection in no way interferes with eventually satisfactory results. It is important to warn the patient of this possibility, however, and to provide an effective anodyne for its control. In general, the more acute the inflammation, the more extensive the infiltration, and the more apprehensive the patient, the greater the risk of this undesirable pain reaction.

Hydrocortisone was usually employed as the acetate. A fairly extensive trial of the free alcohol of hydrocortisone by local injection gave less satisfactory results. In the past year, hydrocortisone *tertiary*-butylacetate has been used both by intraarticular injection, and by the procaine-hydrocortisone infiltration technique for periarticular lesions; results are unpredictable, being better in some, equal in most, and less effective in a few others.

Whatever the anti-inflammatory hormone used, the anatomical vagaries of rheumatic disease must dictate the technique to be used. Intra-articular injection is the technique of choice for straightforward cases, but the differential use of a blended mixture of the test hormone with procaine indicator is essential in about 25%.

*Read at the First Pan-American Rheumatism Congress in Rio de Janeiro, August 15, 1955.

ANATOMICAL NOTES ON THE ORIGIN OF PAIN IN CERTAIN JOINTS (RESULTING FROM USE OF THE DIFFERENTIAL DIAGNOSTIC TECHNIQUE):

1. THE SHOULDER

The subacromial bursa is never connected to the shoulder-joint and, when affected, must always be treated by separate injection: the tendon-sheath of the long head of biceps may be separated fairly early from the shoulder-joint by inflammatory adhesions at the upper part of the "sleeve". Other parts of the fibrous capsule are important but less common sources of pain requiring injection by an "indicator" technique of the type described.

2. ELBOW

When synovial thickening and effusion are not clearly apparent clinically, elbow pain frequently is found to arise from external or internal epicondylitis, or occasionally from periolecranon bursitis.

3. WRIST

Rarely does pain originate in a single compartment: effective treatment of the wrist requires infiltration of hydrocortisone-procaine mixture until local tenderness, and pain on manipulation, are neutralized. Tenosynovitis may even emerge as the principal source of pain, whereas the joint itself may have been previously suspect; but whatever the anatomical source of pain, there are few failures in treatment of the wrist by this method, even in chronic rheumatoid arthritis.

4. KNEE

While synovitis of the knee itself is the most common source of knee pain, inflammation of bursal "cysts" in the popliteal space or below the patella, or inflammation in tendons at their insertions on to the tibial condyles or fibular head, or inflammation of the superior tibio-fibular joint may occur and any of these may explain failure to eradicate knee pain by intra-articular injection. Satisfactory localization and treatment of such foci can only be assured by the indicator-infiltration technique. Not infrequently, it is necessary first to inject the knee-joint itself with a blended mixture of hydrocortisone and procaine, and then to test for pain on manipulation or on weight-bearing, before proceeding to infiltrate other sites in the region that are suspected by clinical examination. In this connection it has proved surprisingly true in most instances that if synovitis of the knee-joint itself is the sole source of pain, intra-articular procaine will (temporarily) abolish the pain almost immediately.

5. ANKLE

Usually, when the ankle region is painful, forced dorsiflexion will reproduce the pain if the ankle-joint itself is at fault. Not infrequently, however, even when the ankle region is swollen and tender, the subastragaloid joint is the major source of trouble. Use of the "indicator" mixture serves to differentiate these two conditions. In other cases of ankle pain, "differential infiltration" of maximally tender regions may show that the source of pain is an Achilles bursitis, subcalcaneal plantaris tendonitis or, not infrequently, medial or dorsal tenosynovitis. When in doubt, the first differential step is to inject the diagnostic mixture directly into the ankle-joint and see whether pain is abolished.

6. OTHER SMALLER ARTICULATIONS

When the hands (or feet) are affected, it may be difficult to decide whether it is the metacarpophalangeal or intermetacarpal joints that are primarily affected; this technique permits satisfactory treatment.

SUMMARY

1. Local injection of hydrocortisone is usually an effective treatment for localized rheumatic pain.

2. To be effective, the hydrocortisone must be brought into contact with the inflamed tissue.

3. Usually, joint pain is due to a synovitis of the joint itself and is therefore amenable to intra-articular injection of hydrocortisone.

4. Not infrequently, however, and particularly in certain joints such as the shoulder, the elbow, wrist and ankle, and occasionally the knee, the lesion responsible for pain is not in the joint itself—and intra-articular injection is not helpful.

5. When the precise location of the source of pain is uncertain clinically, the use of 1% procaine as an indicator, mixed intimately with hydrocortisone ("differential diagnostic infiltration"), has proved of great value both in treatment and in elucidating the sites of pathological disorder.

6. A somewhat increased incidence of painful reaction to injection is to be expected when the infiltration technique is used, but this occurrence does not lessen the proportion of good results.

FORTHCOMING C.M.A. MEETINGS

- 1956 Quebec—June 11-15 (Ecole de Commerce).
- 1957 Regina—June 17-21.
- 1958 Halifax—June 15-19.
- 1959 Edinburgh—July 16-24.
(Conjoint Meeting with B.M.A.)
- 1960 Banff—June 13-17.

The Canadian Medical Association Journal

published twice a month by

THE CANADIAN MEDICAL ASSOCIATION

Editor: S. S. B. GILDER, T.D., M.B., B.S., B.Sc.

Managing Editor: T. C. ROUTLEY, M.D., F.R.C.P.[C.]

Consultant Editor: H. E. MACDERMOT, M.D.,
F.R.C.P.[C.]

Editorial Offices: 150 ST. GEORGE ST., TORONTO

(Information regarding contributions and advertising will
be found on the second page following the reading material.)

Editorials

SURGERY IN MITRAL STENOSIS

On page 940 of this journal we publish an account by Dr. Paul David of Montreal of the indications for and results of mitral commissurotomy performed for mitral stenosis. His findings are based on an analysis of 184 operations, and compare closely in many respects with findings in other series published this year.

Although the operation of mitral commissurotomy or valvotomy has now become a standard and accepted procedure for relief of mitral stenosis, there was an unaccountable hiatus of 23 years between the first reports of successful operations by Cutler and Levine in 1923 and by Souttar in 1925 and the beginning of the present movement in Philadelphia, Boston and London in 1948. Meade¹ in discussing the reasons for this delay suggests that the blame lay with the internists, who refused to believe that good results could be obtained from surgery, and simply did not refer cases to the surgeon. Glover² points out that there are still a few who refuse to believe the patients' accounts of postoperative improvement because of their inability to demonstrate this objectively. Indeed it is a general finding that improvement is more often subjective than objective (murmurs, heart signs, ECG); Goodwin *et al.*³ in analyzing a series of 56 cases note that only one-third of those whose symptoms had improved showed objective evidence of this.

While it is generally agreed that in a majority of instances the operation is extremely successful and an important part of the treatment of cardiac disease,⁴ much depends, as Dr. David shows, on the selection of cases. Age is a factor, and Holmes Sellors⁵ finds 20-50 years the acceptable age group for operation, the patient being left as long as possible after the disappearance of evidence of rheumatic activity. If the American Heart Association's classification of disability into four stages is accepted (Stage I, asymptomatic; Stage II, statically incapacitated; Stage III, progressively incapacitated; Stage IV, terminally incapacitated), most of the candidates for operation will fall into Stages II and III, since the operative mortality rate rises sharply in Stage IV. The presence of auricular fibrillation is not a bar to operation; in the British series reported recently by Baker,⁶ the patients who had had auricular fibrillation actually did better. The presence of disabling and progressive dyspnoea is the chief reason for referral to the surgeon. Goodwin *et al.*³ show that the grade of dyspnoea is correlated with the size of the mitral orifice, and consider repeated attacks of dyspnoea an urgent indication for operation.

Dr. David, like other workers, emphasizes the difficulty of diagnosing mitral regurgitation associated with stenosis. Kirklin and Ellis⁴ state that the most important diagnostic consideration in selection of patients for operation is the detection of *significant* degrees of mitral regurgitation. Whatever the means adopted, differentiation may prove very difficult in some cases. Holmes Sellors⁵ regards embolic episodes as an indication for operation, and Goodwin *et al.*³ recommend patients with repeated embolism for operation, even if dyspnoea is slight. These workers give as the absolute contraindications to operation severe mitral regurgitation, intractable congestive failure, predominant aortic valve disease, and active rheumatic fever—factors also discussed by Dr. David.

REFERENCES

1. MEADE, R. H.: *Surgery*, **38**: 432, 1955.
2. GLOVER, R. P. *et al.*: *J. Thoracic Surg.*, **30**: 436, 1955.
3. GOODWIN, J. F. *et al.*: *Brit. M. J.*, **2**: 573, 1955.
4. KIRKLIN, J. W. AND ELLIS, F. H.: *Surg. Clin. North America*, Aug. 1955.
5. SELLORS, T. H.: *Brit. M. Bull.*, **11**: 208, 1955.
6. BAKER, C. *et al.*: *Brit. M. J.*, **2**: 983, 1955.

Editorial Comments

THE CHANGING MENTAL HOSPITAL

I suppose that few of us would care to bet what a group of doctors would name the single greatest challenge facing medicine today. But whatever their choice might be, one would never have any difficulty in capping it by reminding them (and I fear that in most gatherings of doctors such a reminder would be necessary) of the public mental hospital. The vast numbers of mentally ill people in hospital (there is approximately one mental hospital bed for every general and other sort of hospital bed in North America), the very poor conditions in which most of them are housed, the gross shortages of equipment and staff, and the huge wastefulness and inertia of such a system is something at which the mind of even the most euphoric reformer boggles.

It is discouraging to think about such a dismal inheritance of inadequate buildings, insufficient staff, bad traditions and constant lack of public support. Yet it must be thought about, not merely by psychiatrists and their psychological nursing and other therapeutic colleagues, but by the medical profession as a whole, by the public and by their political representatives. The most costly illnesses are mental illnesses. They are also the hardest to bear. Our inheritance will be a burdensome one whatever we do about it. We can only be sure that in the long run the right moves will be less costly, less wasteful, and cause less suffering than continuing in our present slovenly ways.

Dr. Cunningham Dax's Beattie Smith lectures¹ are an example of the sort of action and thought which is required if we are to cope with the awesome results of about three-quarters of a century's error and neglect. Dr. Dax is Chairman of the Mental Hygiene Authority in Victoria, Australia. He delivered these lectures at the University of Melbourne in September 1954. Before taking up his present position, he and his colleagues at Netherne Hospital, England, developed a therapeutic community whose aim was to encourage mentally sick people to become re-socialized so that they would be once again admitted to the larger community outside the hospital. Clearly, the distilled experience of one who has already shown such outstanding capacity for doing well by his patients cannot fail to be interesting and valuable. Even when one does not wholly agree, disagreement is an exercise bound to widen one's horizon and expand one's mind.

He starts by classifying patients according to their degree of socialization, starting with those who need closest supervision and ending with those who are on open self-governed wards. This is not a new idea, but he is precise and makes many wise comments, of which this is an excellent example: "It is well to have a

minimum of closed wards as the necessity constantly arises to try a number of patients with a greater degree of freedom". He then suggests not merely activities but a social organization appropriate to each group of patients. Those who require little or no supervision should be, indeed must be, self-governed. They must order and arrange their lives, and the hospital must especially beware of degrading them with babying and pampering as so easily happens to "good" patients. However, less well-adjusted patients too must have an opportunity to run their own affairs and so gain social skills and develop interpersonal relationships. In the lectures I missed a discussion of how admission and discharge procedures should be moulded to fit this enlightened approach. I wonder whether we should not go further than Dr. Dax and emulate Topeka State Hospital where there are no admission wards, no untidy wards and no disturbed wards? Patients undertake social activities, but although some wards are closed and some open, they are otherwise much the same. However, in this vast field of human misfortune there is room enough for fruitful experiment. The picture that he paints is of a hospital where patients are kindly but firmly encouraged to accept the responsibility of being people, not chattels or pets.

The second lecture raises two questions. The first is the place of creative activities in the therapeutic community. This alone is so important and fascinating that one cannot possibly do it justice in a brief space. His next question is the future of the mental hospital. He sees in artistic expression a means by which the mentally ill can communicate while in hospital and possibly develop a satisfactory creative activity for when they return home. This again is not new and Dr. Dax does not claim that it is, but he gives an excellent survey of the many men of diverse genius who have been mentally ill and in this way points out his plea that a very wide range of artistic and creative activities is required in mental hospitals. He emphasizes that these are not to be considered luxuries, but essentials, and that the government should be prepared to spend money to encourage people to come and teach. Many young artists have difficulty in getting started and it seems a fine idea that mental hospitals of the future will provide a niche that will tide them over the lean years, with pupils at least as appreciative as many adolescents.

I am less happy with his last section. I do not believe as much as he does in the need for a rigidly stratified hospital. I incline to the view that the great majority of the so-called "deteriorated" cases are the direct result of our present arrangements and that they will disappear with a better policy and buildings designed to meet the needs of the mentally ill. I wish he had given more space to this vital

matter, for I am sure that he has some valuable suggestions. He is very much aware of those grandiose and disastrous old folks' homes with which we are too ready to burden ourselves. Pretentious and oversize buildings are being designed on the specious excuse that they allow "more efficient handling of the geriatric problem". Efficiency is meaningless until one asks, efficient for what? The needs of the old people are soon forgotten in the architect's keenness for something that looks nice and the administrator's search for an economical building. I think, too, he might have made more of one of the most serious gaps in our knowledge—how do people become alienated? Why does one psychotic person become a backward patient in a mental hospital, while another who seems equally ill survives for years, even a life-time, in the community? This vital question is not only unanswered, it is very rarely asked; yet in the answer we are almost certain to discover much information, vital for preventive psychiatry and also for reablement.

As Dr. Dax truly says, the mental hospitals all over the world are at the crossroads, and if those in Australia follow the road towards which he has so clearly directed them, then many sick people will enjoy a very much happier future. Let us hope that other hospitals in other places too will take similar paths and will desert the stereotyped idleness, regimentation and exploitation which has been such a blot on the treatment of the mentally ill for so long. No one who is interested in psychiatry should miss these excellent lectures. I only hope that Dr. Dax has a good supply of reprints. HUMPHRY OSMOND

REFERENCE

1. DAX, E. C.: *M. J. Australia*, 1: 25 and 57, 1955.

ARTIFICIAL RESPIRATION

Dissatisfaction has been expressed from time to time with the lack of exact knowledge of techniques of artificial respiration, not only by the laity but also by a certain proportion of medical practitioners. This of course is associated with the lack of practice in this art, since all but fervent instructors of first-aid groups rarely have need to demonstrate or practise resuscitation. The one field in which a reasonable amount of practice may be obtained is in the resuscitation of small infants, and a recent article by Captain Harold J. Rickard of the United States Navy (*J. A. M. A.*, 159: 754, 1955) sets forth what is claimed to be a new method for manual artificial respiration, in which the shortcomings

of older techniques are overcome. The new method is based on the following premises: (1) speed of initiation is of paramount importance; (2) the prone position is the most desirable one in most cases of asphyxiation; (3) an unobstructed airway is mandatory; (4) the method must be rhythmic and uninterrupted; (5) an adequate pulmonary ventilation must be produced; (6) the possibility of injury by use of uncontrolled external pressure must be eliminated; (7) the pull-push principle, which also favours venous return to the heart, should be used; (8) a single operator should suffice; (9) the procedure should be easy to teach and simple to learn, and (10) it should tire the operator as little as possible.

To maintain an adequate airway, Captain Rickard proposes to employ the Mauriceau manoeuvre as used for extraction of the after-coming head in breech deliveries, by inserting the middle finger of the right hand in the child's mouth over the tongue and drawing the latter forward and downward to provide an airway, while the other fingers support the head on either side of the mandible. The child then straddles the operator's forearm in the prone position, while the operator's left hand is placed palm down across the child's back, with fingers hooking across both shoulders to hold the infant in place. The operator then stands with the child draped along his right forearm parallel to the ground and his upper arm close to the body. The operator may vary his position by kneeling or sitting, with his right elbow on the right patella. Artificial respiration begins with the expiratory phase. The operator lowers his forearm through 45°, so that the abdominal viscera push against the diaphragm and force air out of the lungs, while secretions run out of the mouth. For inspiration the forearm is raised to 45° above the horizontal, and the visceral pull on the diaphragm should suck air in. The rate of tilting should be 8-12 times a minute. As a guide to timing, Captain Rickard suggests that the operator repeat "out goes the bad air, in comes the good air" which will give him a cycle of 12 times a minute. The method can be kept up for 10 to 15 minutes and can be used for children up to 28 lb. in weight. Older children may be treated by cautious use of the Holger Nielsen method.

IMPORTANT NOTICE

Readers of this Journal are asked to note that all departments of the Canadian Medical Association, including the editorial and advertising offices, are now housed at 150 St. George Street, Toronto 5.

REVIEW ARTICLE

CURRENT TRENDS IN THE TREATMENT OF SHOCK*

FRASER N. GURD, M.D., F.R.C.S.[C.],
F.A.C.S., *Montreal*

THE FOLLOWING ARTICLE represents an effort to bring together within the space of a few pages the current trends in the treatment of shock. The majority of recent papers deal with individual aspects of a large and complex subject, while the larger reviews are involved of necessity in a maze of evidence related to etiological factors. The present paper will attempt to offer a brief synthesis of available information directly related to practical treatment.

DIAGNOSTIC ACCURACY

A word should be said at the outset concerning the trend toward greater emphasis on diagnostic accuracy in hypotensive states. This attitude is rendered more significant in the light of the wider range of specific treatments now available for the correction of conditions which may be considered in the differential diagnosis. It becomes clear that the unreasoned use of blood transfusion and other intravenous therapy may delay the institution of more precise and effective measures. The following list is offered as food for reflection, for although each condition may provoke a state of circulatory collapse, replacement therapy has little place in the management of any: sepsis, intracranial damage, intrathoracic injury, pulmonary embolism, massive atelectasis, acute coronary occlusion, vasovagal reflexes, cardiac arrest, and adrenal insufficiency.

Under this heading it should be mentioned that fluid and salt depletion may constitute a cause of shock demanding keen diagnostic acuity. In recognition of this fact, many "unavoidable deaths" of earlier days are now properly classed as "errors of management".

PREVENTION OF SHOCK

In elective surgery, the realization that shock is usually preventable has laid a new responsibility upon the operating surgeon. The answer lies in proper preparation and in the conduct of the operation itself.

The nutritional preparation of the patient is now widely accepted as an important aim, but one not always attainable. Barron and Fallis¹ have shown that many who will not or cannot eat may be realimented by tube feeding with liquefied whole food. Totally parenteral reali-

mentation is still hampered by the limiting factor of providing adequate calories in a reasonable volume of fluid. Pending the development of reliable fat emulsions, we have no certain means of influencing the food storage depots of the patient unable to eat adequately. There is, however, one area of the body economy to which we have direct access, and this is the circulating blood. The preoperative replacement of blood, fluid and electrolyte is a matter over which we do have some control, and little excuse can be offered for permitting a patient to go into shock because of neglect of these factors.

It is now well recognized that the nutritionally depleted individual may have a contraction of total blood volume more or less proportional to his depletion of protein stores. This contraction may not be reflected in the percentage values for haemoglobin or haematocrit. Therefore, regardless of the absence of the conventional indices of anaemia, the patient who has lost weight significantly may require preoperative transfusion as a prophylactic measure against shock. Bigelow and his colleagues have devised a simple formula, to the effect that patients require preoperative transfusion on a scale of 50 c.c. per pound of recent weight loss.² Used within reason, the general plan of giving one bottle of blood for each 10 pounds of weight loss has proved a most valuable preventive of shock at the time of operation.

The trend in surgical training is in the direction of the shock-proof operation. The surgeon must maintain control of the situation at all times, more accidents being due to careless haste than to lack of skill. Losses of blood should be estimated, especially in the poor-risk case undergoing a major operation. The practice of weighing sponges is valuable in this regard. Available blood should be used in anticipation of shock rather than after the event. As an aid in anticipating shock it has been pointed out that a fall in venous blood pressure, recorded from an antecubital vein, precedes the fall in systolic arterial pressure.³ However, clinical alertness by all members of the operative team is preferable to over-reliance upon mechanical aids, except in special circumstances.

TREATMENT

Prevention, as briefly outlined above, is always the best form of therapy. There are times, however, when uncontrolled or unrecognized bleeding, together with such other effects as the disease or trauma may produce, presents us with a picture of established shock. To deal for the moment with the effects of haemorrhage as an entity, there are certain trends which it is timely to discuss.

HÆMORRHAGIC SHOCK

Intra-arterial transfusion enjoyed a period of popularity in the post-war period, based on a

*From the Department of Surgery, McGill University, and the Montreal General Hospital, Montreal, Que.

series of dramatic reports from numerous parts of the world.⁴ Within the last year a group of studies, including our own from McGill, have shed doubt upon its specific advantages.⁵⁻⁷ The technique did render a service to the therapy of shock in so far as it demonstrated that a high rate of flow of the transfused blood was a vital feature of successful resuscitation from severe shock.

The author has published recently a summary of the facts relating to the controversy which has revolved around intra-arterial transfusion.⁸ We are convinced that the treatment of hæmorrhagic shock consists in the introduction of blood into the circulation at any available points which will permit of a rapid rate of flow. The side of the circulation, whether venous or arterial, is of less importance. The introduction of blood under pressure into larger veins such as the common femoral or the external jugular, combined with the principle of multiple streams, will enable rates of flow of 200 to 500 c.c. per minute to be achieved. The weight of evidence suggests that resuscitation at these rates is quite as effective by the intravenous route as by the intra-arterial, and avoids the risk of peripheral gangrene.

With regard to the use of rapid rates of transfusion, one word of warning is in order. We found in our experimental work at McGill that it was possible to overtransfuse if the rapid rate of flow continued as the normovolæmic state was approached. There was danger in maintaining a rapid flow beyond the point of 75% replacement of the shed blood. The danger point was signalled by a secondary fall in the arterial blood pressure after a favourable rise, coupled with a simultaneous rise in the venous pressure to above normal levels. These secondary and unfavourable switches of pressures, if recognized at once, could be corrected by simply slowing or stopping the transfusion.

Our interest in rendering resuscitation effective, and yet subject to safe control, goes back several years to some studies on pulmonary congestion in relation to shock and transfusion.⁹ However, the best advice which has come out of this work is to treat hæmorrhagic shock by very rapid transfusion until a favourable response is obtained, and then to slow the rate of flow until stability is evident.

There are two major possibilities for complete failure of this scheme of management. The first is continued bleeding. Since it requires between one and two litres of blood loss to cause serious shock in a normal adult, replacement of that amount should restore the situation. A good rule to follow is that if a case considered to show pure hæmorrhagic shock fails to respond to a transfusion of between one and two litres of blood, either the patient is still bleeding or the diagnosis is incorrect. The second possible cause of total failure of resuscitation is the dread phenomenon of irreversible shock. Space pro-

hibits any extensive discussion of the many facets of irreversibility, the role of the anoxic liver, the metarteriolar sphincters, depressants such as VDM, bacterial toxins and myocardial failure.¹⁰ The only certain knowledge we possess regarding irreversibility in shock is that it is a function of duration. Beyond a certain point of time, shock becomes incurable by any known method of treatment.

A distinctly radical trend in the management of traumatic shock emerged from the Korean war.¹¹ Artz, Howard and their colleagues report that the American Military Research teams appear to have saved a number of severely wounded men by transfusing extremely large volumes of blood. When five or ten pints of blood failed to effect resuscitation, they pushed on to 20, 30 or even 40 pints, with recovery in several apparently irreversible cases. The really extraordinary finding, from many successive determinations of blood volume, was that these men did not appear to have been over-transfused. The authors felt that in the past we have tended to underestimate the degree of blood loss in severe and multiple wounds, and that the amount of blood lost into the body tissues in the areas of injury is much larger than heretofore suspected. Their extensive studies on the bodily reactions to such extremely vigorous transfusion therapy should be studied by all who have occasion to handle severe injuries. In commenting on these reports of such very massive and apparently valuable transfusions, Ravdin has suggested that norepinephrine (noradrenaline) might assist in obtaining the desired result with greater economy of blood.¹²

The question of transfusion of the elderly patient has come in for considerable study in recent years,¹³ especially in the presence of pre-existing chronic anæmia.¹⁴ Much of the fear of pulmonary congestion has been dissipated by increased experience. There can be no doubt that the elderly may require large transfusions on occasion, and we feel that they should have them. Caution as to the rate of flow and venous pressure, having the patient sit up during administration, and the occasional use of packed red cells are the principal safety factors to be considered.

PLASMA EXPANDERS

Shock following injury is associated with deficiency of available blood volume. The only known method of correction is to introduce into the circulation fluids containing colloids which will remain in the circulation over a considerable period of time. Although the emphasis in the search for the ideal plasma expander is essentially on military and civil defence medicine, situations arise in civilian practice where blood is not immediately available. The problems related to plasma substitutes have concerned the mass production of a material capable of being

sterilized, stored and transported, non-toxic, non-antigenic, without adverse effects on organ function, capable of being excreted or metabolized, of suitable viscosity, of an oncotic pressure equal to plasma, and capable of being retained within the circulation in greater part for at least 12 hours. Molecules of below 30,000 molecular weight escape quickly from the circulation. Those of over 100,000 molecular weight are viscous, are poorly eliminated by the body and interfere with subsequent typing and cross-matching of blood.

At the present time the expander in most general use is dextran. It gives the desired colloid osmotic pressure in 6% solution. It is derived from sucrose by the action of certain bacteria, and as might be expected it is antigenic to a certain degree. Some preparations have been suspected of causing renal damage, and interference with subsequent typing and cross-matching has been reported. However, the preparation at present in use in Canada appears remarkably free from difficulties on fairly extensive clinical trial.¹⁵

Polyvinylpyrrolidone, or PVP, is a synthetic polymer and appears to have few disadvantages. The question of the long-term effects of such portions as are retained in the body has not been fully answered. Gelatins with lower gel points than the early preparations have been developed, and may result in this material's returning into use. More will doubtless be heard soon of human serum albumin, an almost ideal expander, now that the problems of its mass production are being solved.

The field of plasma expanders is in a state of flux, and the most profitable comments to be made concern the principles underlying their use. In short, these materials are temporary plasma expanders only, not blood substitutes. At the same time as they refill the circulation with fluid they diminish the oxygen-carrying function of the blood. Therefore, in hæmorrhagic shock they may be dangerous in that they drive the hæmoglobin value lower. Their greatest usefulness lies in two roles: (1) in maintaining circulation until blood is available; (2) in extending the effectiveness of a limited supply of blood. Used alternately with such units of blood as are available, they may enable operation to be carried through without too much delay.¹⁶

PRESSOR DRUGS

The isolation of lævo-norepinephrine a few years ago resulted in a trend toward the rather free use of pressor drugs in shock. Norepinephrine differs radically from epinephrine in its action.¹⁷ It produces a reliable type of peripheral vasoconstriction which includes the venous side of the circulation. Its effect on peripheral resistance is more favourable to making the best use of available blood volume.

It raises both systolic and diastolic pressures, with some increase in pulse pressure. It does not increase the heart rate in the violent and often ineffective manner associated with epinephrine administration. It may improve the coronary circulation, which has been shown to be doubly embarrassed during shock.¹⁸ Another sympathomimetic amine, known as Aramine, has been shown by Sarnoff to improve coronary flow quite specifically, with a remarkable therapeutic effect on otherwise irreversible shock.¹⁹

Norepinephrine is administered as a continuous drip containing 4 mg. per litre of saline solution. It should not be used during anaesthesia with cyclopropane or in patients with myocardial ischaemia, as it may lead to ventricular fibrillation in such circumstances. Its action is rapid and fleeting and requires constant attendance for its safe control. Care must be taken that it is not employed in the presence of uncontrolled bleeding. Its greatest usefulness is in the patient in whom, by ordinary criteria, the blood volume has been restored by appropriate intravenous therapy, and yet the blood pressure continues at low levels. In such cases it may assist in tiding the patient over for a period, allowing time for intrinsic adjustments within the body, many of which are doubtless still unappreciated, to exert their stabilizing influences. It must be emphasized that it is not a substitute for adequate replacement therapy.²⁰

BURN SHOCK

The treatment of shock in burns applies particularly to the first 48 hours after burning, and to the severely burned patient with skin involvement in excess of 25% of body surface. Treatment consists in a judicious balance between administration of whole blood and other colloids on the one hand, and of crystalloid solutions on the other. The general formula elaborated by Evans in 1952²¹ appears to be standing the test of time. The basis of the Evans formula is that colloidal solutions should be administered during the first 24 hours on a scale of 1 c.c. per kg. \times % of body surface burned. Colloidal solutions include whole blood. Thus, a 70 kg. man with a 30% burn would require about 2,000 c.c. of colloid. Next, this volume of colloid should be matched by an equal volume of electrolyte solution. Finally, glucose and water should be added to ensure a urinary flow of 25 to 50 c.c. per hour. During the second 24 hours the above volumes should be cut in half.

The principal reservation to be kept in mind with respect to the Evans formula is that the calculated volumes may have to be curtailed in very extensive burns. Otherwise overtreatment may result.

The current trend in treatment of shock due to burns relates to modification of the electrolyte

solutions to be used. Winfield, Fox and their co-workers²² have emphasized that the patient with extensive burns tends to become acidotic, and that the use of large volumes of sodium chloride results in the assimilation of too much chloride. Furthermore, the burned patient appears incapable of forming ammonia in the kidneys in the early days after the burn. Accordingly, the elimination of any excess chloride results in the depletion of kation stores, specifically of sodium and potassium, which in turn further aggravates the acidosis. The answer is to use electrolyte solutions which differ from normal saline in that they more nearly mirror the electrolyte balance of plasma. The essential feature of the so-called "balanced solutions" is that they contain more sodium and less chloride.

FUTURE TRENDS

In the field of blood preservation continual progress is being made. Human red cells have been fast-frozen and stored in the frozen state for periods of up to 10 months. Reconstituted, the cells have shown a normal life span in the transfused recipient. The adaptation of mass production methods to this technique of storage still remains to be perfected.

The author's personal impression is that future trends in relation to shock will be heavily involved in pharmacology. Operations previously impracticable because of forbidding blood loss are being undertaken with the help of ganglionic blocking agents. Other operations involving temporary cessation of the circulation are being performed by reducing oxygen requirement through creation of a hypothermic state. Pharmacological hibernation has been suggested as a remedy for shock itself, although still not well substantiated.²³ As to hormonal therapy in shock, the subject is in a state of uncertainty at present. The only definite indication for hormone therapy is in cases where a deficiency of a specific internal secretion can be shown to exist. Serial total eosinophil counts appear to be the most practical index of adrenocortical insufficiency at the present time.²⁴

Finally, there is a trend towards accepting the fact that shock is activated by multiple etiological factors. As Carl Moyer has said, to search for a single cause of shock is like searching for the fountain of youth.²⁵ This concept is of tactical importance in planning an assault on established shock, because it assists us in recognizing that more than one point of attack may be open to us. For example, shock due to peritonitis may call for an attack on a broad front, with virtually simultaneous use of antibiotics, blood, plasma, water, electrolytes, oxygen, intestinal decompression, support of peripheral vascular tone, perhaps support of the hormonal system, and surgical elimination of the focus.

CONCLUSION

In conclusion, one must emphasize that the standard adjuncts to the treatment of shock have not changed. Rest, warmth, posturing, sedation, splinting and maximal oxygenation remain as important as before. Although prevention is better understood, diagnosis more detailed and accurate, and treatment more easily available, it is the human factor of intellectual alertness and energetic corrective action which spells survival for the patient.

REFERENCES

1. BARRON, J. AND FALLIS, L. S.: S. Forum, Proc. of the Forum sessions, Clinical Congress of the American College of Surgeons, W. B. Saunders Co., Philadelphia, 1954, p. 519.
2. BIGELOW, W. G., FLEMING, J. F. R. AND GORNALL, A. G.: *Canad. M. A. J.*, **65**: 37, 1951.
3. PIERCE, V. K., BOYAN, C. P. AND MASTERSON, J. G.: *Surg., Gynec. & Obst.*, **96**: 310, 1953.
4. SEELEY, S. F. AND NELSON, R. M.: *Internat. Abstr. Surg.*, **94**: 209, 1952.
5. CASE, R. B. *et al.*: *J. A. M. A.*, **152**: 208, 1953.
6. MALONEY, J. V. *et al.*: *Surg., Gynec. & Obst.*, **97**: 529, 1953.
7. HAMPSON, L. G., SCOTT, H. J. AND GURD, F. N.: *Ann. Surg.*, **140**: 56, 1954.
8. GURD, F. N. AND GARDNER, C. McG.: *Am. J. Surg.*, **89**: 725, 1955.
9. ROUNTHWAITE, H. L., SCOTT, H. J. AND GURD, F. N.: S. Forum, Proc. of the Forum sessions, Clinical Congress of the American College of Surgeons, W. B. Saunders Co., Philadelphia, 1953, p. 454.
10. RAVDIN, I. S. AND RAVDIN, R. G.: *Internat. Abstr. Surg.*, **100**: 101, 1955.
11. PRENTICE, T. C. *et al.*: *Surg., Gynec. & Obst.*, **99**: 542, 1954.
12. RAVDIN, I. S. AND CASBERG, M. A.: *Am. J. Surg.*, **89**: 721, 1955.
13. GURD, F. N.: *Am. J. Surg.*, **83**: 379, 1952.
14. MITHOEFER, J.: *Am. J. Surg.*, **89**: 740, 1955.
15. WEIL, P. G. AND WEBSTER, D. R.: S. Forum, Proc. of the Forum sessions, Clinical Congress of the American College of Surgeons, W. B. Saunders Co., Philadelphia, 1954, p. 712.
16. SEELEY, S. F. AND PULASKI, E. J.: *Am. J. Surg.*, **85**: 382, 1953.
17. GOODMAN, L. S. AND GILMAN, A.: *The Pharmacological Basis of Therapeutics*, 2nd ed., The Macmillan Co., New York, 1955.
18. EDWARDS, W. S. *et al.*: S. Forum, Proc. of the Forum sessions, Clinical Congress of the American College of Surgeons, W. B. Saunders Co., Philadelphia, 1954, p. 505.
19. SARNOFF, S. J. *et al.*: *Am. J. Physiol.*, **176**: 439, 1954.
20. FREMONT, R. E. *et al.*: *A. M. A. Arch. Surg.*, **68**: 44, 1954.
21. EVANS, E. I. *et al.*: *Ann. Surg.*, **135**: 804, 1952.
22. FOX, C. L., JR. *et al.*: *Am. J. Surg.*, **89**: 730, 1955.
23. CHIPPAUX, C. *et al.*: *Presse Méd.*, **62**: 504, 1954.
24. HAYES, M. A.: *Surgery*, **35**: 174, 1954.
25. MOYER, C. A.: S. Forum, Proc. of the Forum sessions, Clinical Congress of the American College of Surgeons, W. B. Saunders Co., Philadelphia, 1954, p. 465.

USE OF NISENTIL IN UROLOGY: A CLINICAL EVALUATION

Nisentil hydrochloride (di - alpha - 1,3 - dimethyl - 4 - phenyl-4-propion-oxypiperidine hydrochloride) was used successfully by Yow, Mathias and Bunts (*J. Urol.*, **74**: 570, 1955) for 150 unselected patients undergoing such procedures as cystoscopy, urethral dilatation, evacuation of bladder clot, painful catheterization and abscess drainage. Excellent results were obtained in 58% of cases and good results in 34%. Untoward reactions were of no consequence. The dose was 30 mg. intravenously and the drug was used in both inpatients and outpatients. Relaxation and sedation occurred within 30-50 seconds of administration. Nisentil should prove invaluable to urologists.

PUBLIC RELATIONS FORUM

Conducted by L. W. HOLMES,
Assistant Secretary, C.M.A.

VII. DOCTORS AND DOLLARS

THE HUMAN SIDE of medicine collides with the business side when the patient asks: "How much will it cost?" To suggest that this collision need not occur is unrealistic. Almost everyone who incurs doctor, hospital or drug bills has a hidden, if not overt, resentment of these costs. The patient's attitude is "I didn't want to be sick. Now I'm stuck with all these bills."

Paying medical bills is not like paying for a new car or television set or even a new suit. A patient rarely has anything tangible to show for his medical purchase—unless he can find comfort in the scars of his operation! His gratitude for the doctor's services often fades fast once he begins to recover. So the collision *will* take place. A human, realistic approach to the economic aspects of medical care can, however, soften the impact. The following discussion of such an approach draws liberally on material based on the experience of several public-relations-minded doctors.

The patient's complaint about fees stems from (1) the size of the bill, (2) failure to understand the charges made, and (3) methods of collection. In the first two realms misunderstanding can be avoided if physicians discuss medical fees in advance. The third area of friction can be greatly reduced by promoting early payment, proper business practices, assisting the patient in payment, and encouraging membership in prepayment plans.

Doctors traditionally have shied away from financial discussions with patients. But financial gain in medicine is a necessary consideration—albeit subordinate. The doctor is entitled to a just fee and must feel right about charging that fee. By the same token, the patient must learn to accept the doctor's moral right to charge a fee and consider the cost of medicine as a desirable "investment."

The answer lies in a mutual understanding of the financial problems of both doctors and patients. The first step in the development of that understanding is advance discussion of the probable bill. It is here that the provincial schedule of medical fees can be very helpful. It serves to reassure the patient that the proposed charges are standard and reasonable.

The doctor should be prepared to give his patient an estimate of the cost of anticipated care. The physician who believes he soothes his patient, saying "Don't you worry about the money—just concentrate on getting well," is side-stepping his responsibility.

Some doctors give patients an estimate of medical expenses before hospitalization. Such estimates should extend beyond the doctor's own

charges. For example, if a patient is to undergo surgery, the doctor should explain the cost of the operation, the anaesthetist's fee, charges for x-rays and drugs, laboratory fees, home, hospital and office call charges, as well as the approximate hospital bill. This last item is important. People are inclined to blame the doctor for all medical costs, including hospital charges. The advance estimate provides an opportunity to set the record straight.

Discussing fees in advance can help the doctor win his patients' confidence. He can boost his public relations rating even higher by helping patients cut their medical costs.

Cost of illness can be reduced in many ways. First of all the physician should not sell short the office visit. Whenever possible, he should point out to patients that it is more economical for him to treat them in the office than in their home or in the hospital. The telephone helps to reduce home and office calls.

The doctor can reduce medical costs, too, by performing only those tests and procedures which will directly help in diagnosis and treatment. The doctor should have some idea of the cost of the items he is prescribing and work up comparative price lists. This knowledge will help him reduce the patients' drug bills considerably. At the same time he should avoid prescribing drugs in large quantities unless absolutely necessary. Frequently, when he has recovered from his illness, the patient finds himself with drugs left over—drugs he will probably never use again. This is money down the drain.

Then there is the problem of the patient who finds it difficult to meet even the average medical bill. This poses the question: "Reduce the bill or cancel it?" The decision must be the doctor's. There are two prevailing philosophies on this question. One belief is that a doctor should reduce his fee in the hardship case, but not cancel it in order to save the patient's pride; the man who pays a small sum toward his expense does not feel like a charity patient.

The second philosophy is that a doctor should never reduce, but completely cancel a fee if necessary. This evolves from the thought that a doctor should not bargain with his patients about charges.

Here are some suggestions to guide a physician in deciding whether or not a fee should be reduced or cancelled:

1. Get adequate information about the patient's financial status.
2. Encourage advance fee discussions.
3. When a patient requests a lowered fee, investigate locally to find out whether the person is a bona fide needy case or a fake.
4. Determine whether or not needy persons are eligible for public assistance programmes. If so, put them in contact with these groups.
5. When referring patients to another doctor, send financial information.

6. Make financial arrangements which best serve the interest of the patient.

The doctor should help patients to pay their medical bills. There are two ways in which this can be done. One is by providing means by which the patient may spread his payment over a period of time—the instalment plan. The other is encouraging membership in voluntary prepayment health insurance plans.

Instalment buying has become so much a part of our way of life that there is no reason why medical care should not be purchased in the same way. It is not too mercenary to help a patient budget for his medical care.

The instalment method of paying need only apply to large bills. It is generally wise to encourage patients to pay for routine visits before they leave the doctor's office. Promoting pay-as-you-go plans eases the strain on the patient's pocketbook and cuts billing and collecting procedures in the doctor's office. Many people come to the doctor's office prepared to pay but leave without paying because they hesitate to bring the subject up themselves. The doctor can smooth the way and relieve the patient's uncertainty by saying at the end of the visit: "My usual charge for an office call is \$3. If you would like to pay today, please stop at my secretary's desk as you leave." Or, when the patient stops at the secretary's desk to make another appointment, she can say: "Would you like to pay for your visit today?" as she reaches for her receipt book.

Payment plans can be handled in the doctor's own office by him or his secretary. For example, in fixed fee cases such as baby inoculations, it is easy to work out an instalment plan merely by dividing the total sum by the probable number of calls or number of months during which the care will be provided and asking the patient to pay a portion of the sum at monthly intervals or at each visit.

Let us imagine a patient comes to the doctor's office during the third month of pregnancy. She can work out a seven-month payment plan with the doctor and make her last payment correspond with her last postnatal visit.

The instalment plan may also be used for patients who are behind in payments. Instead of mailing out monthly bills, the doctor might send out a small card worded something like this: "Rather than mail you your statement, I am sending you this card so you may remit small monthly payments to clear up your account. Just return your cheque or a cash amount with this card, and we will receipt it and return it again next month." This informal approach eliminates the fear and antagonism engendered by threatening collection letters. It also provides an "out" for the patient who is embarrassed by a long-overdue account.

The second method of payment—the voluntary prepayment plan—is the profession's own ap-

proach to the problem of meeting the cost of medical care. Each year the number of subscribers to such plans increases by thousands. Every doctor can help promote these plans to his patients and in so doing helps them and the profession. It is an especially good idea to recommend membership in the plans to slow-paying patients or to those who seem to be having financial difficulty.

The doctor must, of course, guard against overuse of the prepayment plans. He must do so to protect his own interests as well as those of the patient. If they are abused, premium rates could rise to a prohibitive point at which the law of diminishing returns would become active. Subscribers would drop away and add their voices to the clamour for national health insurance.

A final word on the doctor's bill. For years these were sent out bearing the familiar phrase "To Professional Services", the sum owed and nothing more. Often bills were mailed irregularly—sometimes not sent out at all. Today people expect to receive statements for their purchases. Most of them plan their budgets around first-of-the-month bills. This suggests that the doctor must do two things:

1. Send bills regularly.
2. Itemize charges.

Patients are entitled to know what charges are for. It is also good business and good public relations. As time elapses after treatment, the patient may forget that he was treated at the doctor's office four times instead of three. On the surface of the unitemized bill it may appear to him that he has been overcharged.

The simplest method of itemizing bills is to allow space below "To Professional Services" on which to list the separate charges for office, house and hospital calls and for tests and treatment.

Punctuality in billing encourages prompt payment. If the doctor is negligent and doesn't send a bill for several months after treatment, the patient may justifiably deduce that the doctor doesn't attach much importance to the bill and postpone payment, sometimes indefinitely.

Human nature being what it is, there will always be delinquents on the physician's books. Suggestions for good public relations, practices in collecting overdue accounts, will be discussed in the eighth article in this series.

CHANGE OF ADDRESS

Subscribers should notify the Canadian Medical Association of their change of address *two* months before the date on which it becomes effective, in order that they may receive the *Journal* without interruption. The coupon on page 61 is for your convenience.

GENERAL PRACTICE

HÆMATURIA*

A. W. BADENOCH,† M.A., M.D., Ch.M.,
F.R.C.S., London, Eng.

I MAKE NO APOLOGY for a paper about a symptom. Hæmaturia is comparatively common, is usually obvious to the patient and, since it may be the first indication of a serious malady, should always receive attention. There are few patients who are not worried when they see blood in a freshly voided specimen of urine and the large majority seek medical advice. It is therefore most important that we should not fail them. Every case of hæmaturia requires investigation, although it is not always either necessary or beneficial that such investigation should be a complete overhaul of the urinary tract, as this can be involved, expensive and unpleasant. In assessing the scope of investigation, attention as ever must be paid to the history, to the age and to the sex of the patient as well as to the physical examination. It is not of course, always possible to arrange the cases in watertight compartments, but apart from those associated with trauma there are three main groups:

1. When the hæmaturia is associated with abdominal pain.
2. When the hæmaturia is associated with urgent, frequent or painful micturition of recent occurrence.
3. When the hæmaturia is not associated with other symptoms.

In the first group the pain may be abdominal; it may be in the back or may be typical of a ureteric colic radiating from the loin to the external genitalia. It may have preceded or accompanied the hæmaturia, and the diagnosis is then almost certainly a stone and usually a moving stone. Such a case requires an x-ray examination; a survey film is taken to determine whether there is a stone, and its size and position, and an excretion urogram is made to show what effect the stone is having on the renal function, and to determine any abnormality of the tract which may be present.

Hæmaturia occurring with frequent painful micturition is almost always due to an acute urinary infection by an organism such as *Bact. coli* or *Streptococcus faecalis* and only rarely to *Myco. tuberculosis*. There has usually been marked frequency of micturition for 12-48 hours, together with burning during the act and pain at the end. Bleeding is often profuse, however,

and may be the predominant feature. It frequently occurs at the end of micturition and there is no doubt from the history that it comes from the lower urinary tract. A specimen of urine should be examined; the deposit, preferably centrifuged, is microscopied and will be seen to contain an excess of leukocytes and organisms. A culture is set up and the sensitivity of any organism grown is determined. Whilst awaiting this result, copious fluids, an alkaline diuretic and a sulphonamide are administered. If bleeding has been the main feature, it is probably safer to cystoscope the patient after the infection has been eradicated, but if it has only been an incident in an obvious acute cystitis, this examination is unnecessary.

The third group contains the majority of cases and a discussion of these is the main purpose of this paper. In an adult, painless, spontaneous hæmaturia if untreated nearly always recurs, and recurs periodically. The amount may be slight or profuse. The cause may be some trivial condition such as a ruptured submucous vessel but, until proved otherwise, may just as well be a cancer of the kidney or bladder which will certainly greatly shorten the life of the patient if untreated and may still do so despite surgical intervention. Three males have painless hæmaturia to every one female. In a high proportion the cause is a neoplasm of the urinary tract. In a series of 1,000 cases of hæmaturia analyzed by Riches,³ 56% of the total were suffering from a tumour and in those who present with hæmaturia as the sole symptom, a neoplasm is found to be the cause in 70% of cases. It is essential therefore that in this group a full endoscopic, radiological and sometimes hæmatological survey should be undertaken until the cause is ascertained.

Cystoscopy is essential in all cases of painless hæmaturia and should if practicable always be done when the patient is bleeding—that, of course, does not mean that the examination should be postponed if bleeding has ceased by the time the patient is seen. If the cause is in the bladder, it will be apparent except when bleeding is so excessive that visibility is obscured. If the cause is in the upper urinary tract, blood is seen in the ureteric efflux, and the side of the lesion is pin-pointed straightaway. A radiograph may show a stone which can cause painless hæmaturia, and excretion urography, which will always be done, may prove the presence of a lesion in the upper urinary tract and help to determine the treatment of a lesion of the bladder. If by cystoscopy and excretion urography the origin of the bleeding has not been determined, a bilateral retrograde pyelogram will be necessary.

RENAL CAUSES OF HÆMATURIA

In about 25% of cases of painless hæmaturia, the origin is in the kidney. This organ is not

*Paper read at the B.M.A., C.M.A., O.M.A. Annual Meeting, Toronto, June, 1955.

†Surgeon to the Royal Hospital of St. Bartholomew; Surgeon to St. Peter's Hospital for Stone; Urologist to the Royal Masonic Hospital, London.

a very common site of tumour formation and in the five-year period, 1947-1952, only 45 renal tumours were found in 4,698 malignant neoplasms at St. Bartholomew's Hospital. Ten per cent of the neoplasms in Riches' series were located in the kidney. Bleeding occurs spontaneously and the urine passed is the same colour throughout. Occasionally the hæmaturia may be so profuse as to cause clot retention but this is most uncommon on the first occasion. Rarely, small clots, which sometimes resemble tea-leaves, may be passed in an otherwise clear urine and this is very suggestive of an upper urinary tract origin. These may occur without anything in the nature of renal colic. In a third of the cases of adenocarcinoma, an enlarged kidney can be felt, and this is so in a higher proportion of cases of embryoma or nephroblastoma, which is the only tumour found in children. Unless there is an associated hydronephrosis, the kidney can rarely be felt with a tumour of the renal pelvis. On excretion urography a soft tissue tumour may be detected alongside the kidney or there may be displacement or distortion of a calyx. In the more advanced case, there will be destruction of part of the pelvis and calyceal group, and in some there is no evidence of a functioning kidney, which is suggestive of involvement of the renal vein. When there is no excretion a retrograde examination is essential and should nearly always establish the diagnosis of a renal or ureteric neoplasm. Occasionally it may be impossible on pyelography to distinguish whether a space-filling lesion is a cyst or a neoplasm. In such a case help may be obtained from an aortogram, as lacking of the blood suggests tumour, and diminished supply, a cyst. A small lesion such as a filling defect in the pelvis may be demonstrated by retrograde examination. This can be caused by a non-opaque uric acid stone which is suggested when the margin is clear-cut, or a papilloma of the renal pelvis if the outline is a little shaggy.

There are cases, however, when a bloody efflux can be seen from a ureteric orifice and yet the appearance on excretion and retrograde pyelograms is completely normal. When bleeding is unilateral there is sometimes an indication for surgical intervention. Occasionally persistent blood loss may produce anæmia or the patient may have bouts of pain accompanying the bleeding. Rarely, a clot in the pelvis may give rise to a filling defect on a pyelogram. Any form of conservative exploration is likely to be unsatisfactory. If there is a lesion present which can be seen or felt in an exposed kidney, it is probable that this lesion can be demonstrated radiologically before operation. Exploration of such a case, therefore, usually means nephrectomy. In more than half the cases there is then a demonstrable pathological lesion for the bleeding, such as an angioma or adenoma or occasion-

ally a small tuberculous focus.² None of these lesions is serious and when such a kidney has been removed one wonders whether the operation has been necessary. On the other hand, as long as unilateral bleeding continues there can be no certainty that the cause is not malignant or potentially so. In some cases blood may be seen coming from each ureteric orifice, and the correct diagnosis may not be made until autopsy. Amongst conditions which have given rise to bilateral renal bleeding are congenital polycystic disease, which can generally be diagnosed by finding a renal tumour on each side and by the typical pyelographic appearance. Nephritis and nephrosis are suggested by other signs and by the presence of casts in the urine; hypertension is diagnosed by the raised blood pressure and the elimination of other causes, and purpuric manifestation is suggested by an abnormal blood picture or bleeding arising from other mucous membranes.

BLADDER CAUSES OF HÆMATURIA

Bladder tumours are the commonest cause of symptomless hæmaturia, being responsible for 60% of cases. The large majority are epithelial and arise in the mucous membrane. If a growth has not spread into the muscle of the bladder it can be destroyed and its otherwise inevitable course controlled. If it has infiltrated into the muscle this is by no means certain and if it has spread through the bladder, removal or control will always be doubtful. Early diagnosis is therefore most important and on cystoscopy a diagnosis will be established. A bimanual examination, which except in the thin co-operative patient must be done under full anæsthesia, will give a useful indication of the extent of spread. If the growth is fixed to the wall of the pelvis, treatment is doomed to failure. If the growth cannot be felt, full control can be anticipated, but between these extremes much may still be done. A radiological examination will show infiltration of the wall by a "bite" deformity or by stasis and dilatation in one ureter. A cystogram may reveal an unsuspected diverticulum with a filling deformity from a carcinoma. Finally a biopsy will confirm the histological grade of the tumour and may help in deciding whether surgery, irradiation or both is the most hopeful treatment. A bladder tumour, be it malignant or benign, although the commonest lower urinary tract lesion to produce bleeding, is not the only one. Not infrequently (15%) the bleeding is from an enlarged prostate which, though more often benign, may be malignant. There is, of course, usually some other symptom of prostatic obstruction such as nocturnal frequency of micturition or difficulty in starting, and the enlargement in such a case can always be felt on rectal examination. Bleeding may be quite profuse, although usually it is not, and occurs either at the commencement or at the very end of the act of

micturition, but beware of incriminating the prostate before eliminating the presence of a neoplasm elsewhere. Lastly, a foreign body in the bladder may cause bleeding. If it is a primary stone, pain and strangury will usually accompany the hæmaturia. If as is more usual the stone is secondary to a lower urinary obstruction, it will be cushioned by residual urine and will be painless. A foreign body which has been introduced by the patient may be a cause. More often than not the patient admits to its introduction and some object, often quite common, such as a hairpin, safety pin or leather bootlace, although in an unusual situation, is easily recognized on cystoscopy.

CONCLUSION

We must therefore take cognizance of the red sign of danger. Remember that although the bleeding will always stop of its own accord, in nearly every case it will recur. Without adequate investigation, it is pure speculation to hazard a guess as to why the bleeding has occurred. In some the diagnosis is easily made, in others it requires perseverance on the part of both doctor and patient, but the diagnosis must be made, for then and then only can correct treatment be administered.

REFERENCES

1. BADENOCH, A. W.: *Ann. Roy. Coll. Surgeons England*, 16: 163, 1955.
2. DUKES, C. E.: *Tr. M. Soc. London*, 65: 375, 1949.
3. RICHES, E. W.: *Ibid.*, 70: 1, 1954.

COURSE IN DERMATOLOGY



THE POSTGRADUATE Education Committee of the Department of General Practice of the New Mount Sinai Hospital, Toronto, has arranged a postgraduate course in dermatology in co-operation with the section of

dermatology of the Department of Medicine. This will consist of lectures given each Friday morning from 9-10 a.m. starting January 6, 1956. The lectures will be followed by demonstrations of interesting cases from the Dermatology Clinic or ward, and will take place in the auditorium of the Hospital at 550 University Avenue. This course has been approved by the College of General Practice for 14 hours of formal study credits. Two hundred doctors may be accommodated.

Physicians interested in registering for this course should write to Dr. M. Herman, 1573 Eglinton Avenue West, Toronto, and enclose a cheque for \$10 made out to the Postgraduate Education Committee, the New Mount Sinai Hospital.

POSTGRADUATE COURSES, DALHOUSIE UNIVERSITY

The Postgraduate Committee of Dalhousie University announces the following courses:

Short Course in Psychiatry—January 30, 31 and February 1, 1956. Fee \$15.

Short Course in Anaesthesia—February 27, 28, 29 and March 1. \$20.

Week in Medicine—featuring Rheumatism and Arthritis and Neurology—March 26-30. \$25.

Two-Day Symposium in Dermatology—April 9 and 10. \$10.

Week in Surgery—April 23-27. \$25.

Obstetrics and Gynaecology—May 7, 8 and 9. \$5 per day.

Pædiatrics—May 9, 10 and 11. \$5 per day.

Information about these courses may be obtained from the Executive Officer, Postgraduate Committee, Victoria General Hospital, Halifax, N.S.

MEDICO-LEGAL

FOREIGN BODIES: LOST RUBBER DAM

T. L. FISHER,* M.D., Ottawa

IN MAY 1953, a doctor dissected a thyroglossal cyst out of a two-year-old boy. At the end of the operation he put in the wound a short strip of rubber dam affixed to the skin edge with a Michel clip; a gauze dressing was applied and fixed with adhesive tape. The following morning there were no dressings on the boy's neck, the rubber dam was not visible but all the clips were present. The doctor learned that the original dressing had been taken off by the boy and discarded by the night nurse who reapplied another dressing which in turn had been pulled off by the child. She did not remember whether or not she had seen the drain.

The wound healed well, the child was discharged from hospital and nothing unusual was noticed until the second week in August when a swelling appeared. This was examined several times. Some mucinous but not purulent material was aspirated on two occasions and then the wound broke down. In mid-September the rubber drain was discovered and removed.

In May 1954, a writ was issued claiming special and general damages because of "the negligence of the defendant in failing to take reasonable precautions before, at the time of or after a surgical operation performed by the defendant . . . for the removal of a thyroglossal tumour, in order to prevent a rubber dam inserted for drainage purposes in the operative

*Secretary-Treasurer, Canadian Medical Protective Association.

wound in the neck of the said infant plaintiff from dislodging and entering the neck. . ."

The case was tried before Mr. Justice Whitaker of the Supreme Court of British Columbia on March 1 and 2, 1955, and judgment was reserved. On May 10, 1955, the action against the doctor was dismissed. The following were the reasons for judgment:

The evidence leads me to the conclusion that the rubber drain was released from the clip when the bandage which had been applied by the defendant was torn away by the infant plaintiff, or by the child plucking at the protruding end of the drain after he had torn the bandage off. Even if it could be said that *res ipsa loquitur* applies, and I think it cannot, the evidence of the defendant and of other witnesses satisfies me that there was no negligence on the part of the defendant, in the method used to affix the drain in the first instance, or in failing to discover that the drain had become lodged in the wound; nor do I think the defendant can be held accountable for the failure to use more effective methods of preventing the child from reaching the bandage with his hands.

The first specific act of negligence alleged in the statement of claim is failure, immediately following the operation, to secure the rubber drain in such a way as to prevent it from disappearing into the wound.

The edges of the wound were held together by means of Michel clips. The drain was fastened as shown in exhibit 2. One prong of the clip holding the drain penetrated both the drain and the skin. All the doctors who gave evidence say this is one of the three methods commonly used and is an acceptable and recognized procedure. Dr. N. says he does not usually secure the drain at all, relying on the mucus oozing from the wound to act as a mucilage causing the drain to adhere to the gauze of the dressing.

Dr. G. said that on his first post-operative visit at 10:30 a.m. on May 31, the bandage was on the floor and there was no sign of the rubber drain. He said the central two or three clips were loose but they were holding the skin together and it was not necessary to replace them. Presumably the drain had originally been fastened by one of the clips found by the defendant to be loose. It is difficult to see how both ends of that clip could be found holding the skin together after the drain had been torn away. A possible explanation is that the clip had been readjusted by the nurse who put on the fresh bandage earlier that morning; or the defendant may not have noticed that one end of one of the clips was not attached to the skin. In any event, I accept without question Dr. G.'s testimony that the drain was properly secured by means of a clip before the infant plaintiff was removed from the operating room.

The next specific act of negligence alleged is that the defendant failed to probe the wound before the child was discharged from the hospital, in order to ascertain whether the drain was lodged in the wound.

When the defendant paid his first post-operative visit on the morning following that of the operation he found the bandage lying on the floor. There was no sign of the rubber drain. The defendant spoke to the nurse in charge. They both consulted the chart. The chart said nothing about the drain. They consulted the notes made by the nurse who had been in attendance. Those notes disclosed that the child had torn off the dressing at 5 o'clock that morning, but there was no mention of the drain. After making all possible enquiries and examining the wound externally the defendant came to the conclusion that the drain must have come away with the dressing; that the chance that it might have gone into the wound was so remote he would not be justified in probing the wound. He came to that conclusion:

1. Because of the remoteness of the chance that the drain would become embedded in the type of wound;
2. Because of the danger of damaging tissue by probing and of introducing new infection and of activating infection already in the wound; and

3. Because he felt the presence of a foreign body in the wound would become manifest either before the child left hospital or within a period of two weeks following the operation.

These would seem, to a layman, to be very cogent reasons, and they are all supported by Dr. N., a very eminent surgeon, who says he would have done exactly as the defendant did. In addition, the plaintiff's expert witness, Dr. A., said he would not want to open the wound unless necessary.

The only other specific act of negligence alleged is that the defendant failed to take steps to see that the child was adequately restrained. The method used by the nurses was a harness which, however, did not prevent the child raising his hands to his neck. It is not for me to make a finding of negligence, unless such negligence is to be imputed to the defendant. In effect, the evidence is that complete restraint, as by tying the child's hands to the sides of the crib, is apt to have a bad effect on the patient, and is to be used only when necessary. The necessity for such restraint can be judged only by those who have, or ought to have, the patient under their constant observation and care following the operation. For them, the exercise of such judgment, and the use of such methods as the occasion may seem to require, are matters of routine. It is not necessary for the operating surgeon to issue specific instructions. Dr. N. was asked:

Q. "What is your practice with respect to restraining a child two years old that has undergone an operation of that nature?"

A. "There are no standing orders for it, sir. That's more or less the responsibility of the trained nurses we have there for the child—lots of children have operations on their neck and don't require restraint, and some must do. There is no standard procedure."

Q. "Does the doctor give instruction to the nurses about that?"

A. "No, he is not of necessity there when the restraint becomes necessary."

In these days of busy surgeons and up-to-date hospitals that would appear to be only common sense.

The action must be dismissed.

Association Notes

REUNION A QUEBEC

LA VILLE DE QUÉBEC se réjouit à la pensée d'accueillir dans ses murs le prochain Congrès de l'Association Médicale Canadienne.

Fait ignoré par plusieurs c'est à Québec, que fut fondé, en 1867, l'Association Médicale Canadienne. Le prochain Congrès prend donc un peu l'aspect d'un pèlerinage au pays natal.

Depuis plusieurs mois, les différents comités sont à l'œuvre pour l'élaboration d'un programme scientifique digne des précédentes réunions annuelles.

Nous voyons dans ce Congrès l'occasion d'échanges scientifiques et culturels d'une portée considérable.

Nul doute que tous nos confrères de langue française partageront cet enthousiasme.

Une nombreuse assistance est prévue et tous les médecins de la Province de Québec, membre ou non de l'Association Médicale Canadienne, seront les bienvenus.

QUEBEC MEETING

THE OLD CITY OF QUEBEC, founded in 1608 by Champlain, looks forward with the greatest pleasure to the annual meeting of the Canadian Medical Association to be held next June within its walls — walls which have witnessed so many other memorable events.

It was in Quebec in 1938 that King George VI, and some years later Her Gracious Majesty Queen Elizabeth, were welcomed in Canada. During the last War, the Citadel of Quebec was chosen by Roosevelt and Churchill for one of their meetings. And finally, a fact that many are not aware of, the Canadian Medical Association was founded in Quebec, in 1867, so that the next meeting may be considered as a bit of a pilgrimage to the native land.

For several months, the different committees have been working at the elaboration of a programme worthy of previous annual meetings. The President-Elect, Dr. R. Lemieux, and the members of the Quebec Division hope that this Congress will be the occasion for a scientific and cultural exchange of great importance. They have no doubt that all members will be pleased with the choice of Quebec City for this congress. Besides the points enumerated above, everyone will find that tourist interest which has conquered the hearts of so many visitors. The Committee on Entertainment will help in visits to historic sites.

Those who would like to take their holidays at the same time can get all the necessary information from this committee.

As a large attendance is anticipated, we suggest that each one begin thinking about this important meeting now.

SCIENTIFIC EXHIBITS

Annual Meeting-C.M.A.

Quebec City, June 11-16, 1956

LIMITED SPACE is available for scientific exhibits. In writing for an application form, please give some details regarding the subject, type of exhibit, approximate floor and wall space required and any extra equipment required. Application should be made before March 1, 1956 to: Dr. Carlton Auger, Department of Pathology, Laval University, Quebec City, Que.

INTERLUDE IN THE PRESIDENTIAL TOUR— NEWFOUNDLAND, 1955

Drs. T. C. Routley and A. F. W. Peart are initiated into the mysteries of jigging for cod by Dr. R. J. Simms of St. John's.

Before:



During:



After:



PRESIDENTIAL VISIT TO ENGLAND

IN THE COURSE of his duties as President of the British Medical Association, Dr. T. C. Routley attended the November meeting of the Council of the B.M.A. in London, England. He expressed himself as amazed at the amount of business that the B.M.A. Council had to get through and was very laudatory of the detailed and careful preparation for the meeting which had been done by the Secretary, Dr. Macrae, and his staff.

At the conclusion of the meeting a Council Dinner was held in the Great Hall of B.M.A. House, London, on November 4 in honour of the six eminent members of the medical profession of the Soviet Union who had that day concluded a three-week visit to the United Kingdom as guests of the B.M.A. As President of the Association, Dr. Routley received the guests, who included the Minister of Health, the President of the Royal College of Physicians, the President of the Royal Society of Medicine, the Secretary of the Medical Research Council and numerous representatives of learned societies and government departments. The Soviet visitors were: Professor S. A. Sarkisov, Director of the Scientific Brain Institute of the U.S.S.R.; Professor V. V. Kovanov, Director of the School of Operative Surgery and Topographical Anatomy of the first Moscow Order of Lenin Medical Institute; Professor G. F. Gause, Deputy Director of the Institute of Research for New Antibiotics; Professor L. F. Larionov, Director of a department of the Institute of Experimental Pathology and Therapeutics of Cancer; Professor M. N. Foteeva, Director of the Biophysical Laboratory of the Institute of Therapy; Dr. L. G. Bogomolova, Director of the Laboratory of Blood Transfusion, Leningrad Institute.

They had for three weeks been making an intensive study of medical organizations in London, Oxford, Cambridge, Edinburgh, Glasgow and Birmingham, and had exchanged experiences with their British colleagues in many fields of medical science. They had, in addition, been given the opportunity to visit various historical and cultural institutions in Britain. At the conclusion of the dinner the Russian delegation was given a film illustrating corneal grafting, from the B.M.A. Film Library, and they, in turn, presented to the Association a number of gifts, including an arterial suture machine and other surgical instruments.

AMENDMENTS TO D.V.A. SCHEDULE OF MEDICAL FEES

NEGOTIATIONS have been proceeding for several months with the Department of Veterans' Affairs with a view to achieving an upward revision of

the schedule of medical fees relating to physicians' visits. The schedule was last revised in 1954 and it was the view of the Canadian Medical Association that the increases then authorized were inadequate in the light of current costs of practice.

Information has been received that, effective January 1, 1956, the Treasury Board has authorized the following schedule to apply to services rendered to entitled veterans under the doctor-of-choice plan:

- (a) Office—Day Visit—\$3.00.
- (b) House—Day Visit—\$4.00.
- Night, Sunday and Emergency—\$5.50.

CANADIAN INTERN PLACEMENT SERVICE

ONE of the most useful activities of the Canadian Association of Medical Students and Interns is the operation of the Canadian Intern Placement Service. The system operates to provide an orderly and systematic method whereby the current graduates of participating Canadian medical schools may seek their initial internships in Canadian hospitals approved by the C.M.A. for the training of interns. Freedom of choice by senior medical students and freedom of choice by the participating hospitals are the essentials of the plan. As the number of approved internships greatly exceeds the current output of Canadian medical schools no system can supply all hospitals with the number of interns they desire. Despite this fundamental limitation, C.I.P.S. provides a far more equitable distribution of the available interns than any other system yet devised on a national scale.

Reporting to the Annual Conference of CAMSI, Mr. M. E. Graham, student Secretary-Treasurer of C.I.P.S., stated that 373 graduates of the class of 1955 at six participating medical schools had been placed in internship in 36 Canadian hospitals; 91% of students using the service had been placed in the hospital of their first choice, 6% in their second choice, 2.5% in their third choice and none were unplaced. It is estimated that 102 students of these medical schools sought and obtained their first internships in the United States.

At five Canadian medical schools degrees are not awarded until after the first internship and students are directed to hospital appointments in institutions affiliated with the university. The graduates of these schools do not participate in C.I.P.S.

Although the C.I.P.S. system of appointments is simple and straightforward, it depends on the co-operation of a large number of individuals. It is perhaps too much to expect that some hospital administrators will not seek their own advantage

by extracting pledges from likely applicants, thus nullifying the element of free choice, and that some students will not change their minds after assignment, thus bringing into discredit the individual and the system. These are the exceptions and it is evident that a substantial majority of hospitals and students find in C.I.P.S. a satisfactory method of arranging for the all-important first internship.

As the Service swings into action for the current academic year, students are seeking information about the training available to them in hospitals from coast to coast. Teaching hospitals naturally occupy a preferred position, but approved hospitals remote from universities can attract interns by providing supervised instruction by an interested and well-organized medical staff and adequate publicity directed towards the students.

MEDICAL SOCIETIES

COLLOQUE INTERNATIONAL ON CHLORPROMAZINE AND THE NEUROLEPTIC DRUGS

An international conference on the clinical and pharmacological aspects of chlorpromazine, reserpine and related drugs was held in Paris, France, October 20-22. The conference was called by the Medical Faculty of the University of Paris and was organized by the Chairman of the Department of Psychiatry, Professor Jean Delay, who is Director of the Centre Psychiatrique at St. Anne Hospital, Paris.

Representatives from 25 countries had been invited and had come to Paris, some of them from as far away as Peru and Mexico. Three representatives from the United States and three from Canada presented papers at the conference. Dr. L. Larue, Medical Director, Saint-Michel-Archange Hospital, Mastai, Que., acted as chairman at one of the sessions. The meetings were held in the lecture room of the St. Anne Psychiatric Hospital, which is about half an hour's drive by taxi from the Opera and the centrally located hotels in Paris.

The St. Anne Hospital has a long history and a fine psychiatric tradition. Its buildings are old and the lecture room was just large enough to hold the audience of about 150. A great deal of planning had gone into the organization of the meeting. Papers were to be delivered in four languages—French, English, German, Italian—and simultaneous interpretation into French and English was available not only in the conference room but also by personal portable receiver elsewhere in the building or grounds.

As there were 112 speakers on the programme and (counting the discussants) 142 different presentations were given during the three days, each paper was limited to eight minutes and the chairmen generally held the speakers strictly to the allotted time. The fast pace at which the papers were delivered and their conciseness made them sometimes difficult to follow, particularly toward the end of the day. All contributions will, however, be published in one volume and many of them in somewhat extended form.

Most of the contributions dealt with chlorpromazine, but about 20 reports considered reserpine. A few speakers made reference to new drugs with similar therapeutic effects such as Atarax and A Y 5406-1 which have not

yet emerged from the experimental stages and might possibly produce serious complications (Busscher). Some time was spent on discussion of a generic name for these new therapeutic agents in psychiatry, and the term "neuroplegic drugs" was proposed by Delay and Deniker, who were the first to introduce such a drug (chlorpromazine) into psychiatry three years ago.

A few reports dealt with the mode of administration. While most clinicians rely on intramuscular and oral administration, hibernation methods employing cooling of the patient and the use of a mixture of drugs with effects on the central and autonomic nervous system in addition to chlorpromazine were described by some speakers (Ey *et al.*; Picard *et al.*; Neveu). Hibernation seems to be a difficult and somewhat risky procedure. Continuous intravenous perfusion with chlorpromazine in states of acute excitement was recommended as a comparatively simple and safe (Lecomte *et al.*) method of administration.

There seemed to be general agreement about the principal indications for chlorpromazine in psychiatry; namely, manic states; acute psychotic breakdowns associated with psychomotor excitement; anxiety and panic states; psychosomatic conditions; delirium tremens and other toxic-confusional states. Newer therapeutic applications of chlorpromazine were reported in Huntington's chorea (Walter-Buel) and in porphyria (Coulonjou).

Of particular interest were the reports on the therapeutic effectiveness of chlorpromazine and reserpine in chronic schizophrenia. There was considerable agreement that these drugs may either prevent chronicity or modify it in such a manner that social recoveries may be obtained in a good proportion (35-75%) of chronic patients (Delay and Deniker; Schneider; Racamier; Staehelin and Labhardt . . .) kept on maintenance doses of the drug after leaving the hospital. Hyvert found that his female chronic patients responded better than his male and was able to improve his therapeutic results with male patients by giving them oestrogens with the chlorpromazine. Watt had done a carefully controlled investigation on 24 chronic schizophrenics, alternating chlorpromazine, placebo and reserpine, and came to the conclusion that only chlorpromazine was therapeutically effective in his series. The comparatively small number of cases treated and the short periods of time (six weeks) during which patients were kept on each drug must be considered in finally evaluating his results.

Rees observed that patients who in the Funkenstein test could be classified in groups 1, 2 or 6, i.e. those who reacted strongly to adrenaline or mecholyl, had a better prognosis with chlorpromazine, while Ey *et al.* noted that schizophrenic patients with discontinuous alpha rhythm in their electroencephalogram responded less favourably than those with continuous alpha rhythm. Bonnet observed that patients with a high threshold to photic driving and photomyoclonic response react better than those with a low threshold.

A number of reports dealt with the use of chlorpromazine in epilepsy. The drug seems to lower the convulsive threshold and thus increase the tendency to seizures. However, in combination with barbiturates or other anti-convulsant drugs chlorpromazine often proves useful in myoclonic epilepsy and in behaviour disorders associated with epilepsy. Delgado reported on clinical experience with the drug in Peru, and Falcon on its psychiatric use in Mexico.

Bleuler suggested guides for the therapeutic application of chlorpromazine and reserpine. While chlorpromazine is faster acting than reserpine, he feels that it is relatively contraindicated in patients with suspected liver damage. Reserpine, on the other hand, is in his opinion contraindicated in cases in which extrapyramidal damage or stomach disturbances are suspected.

Overholser pointed to the changes that may be brought about in mental hospitals by the new drugs. Mayer-Gross discussed the possibilities of future pharmacological discoveries in psychiatry and stressed the need for carefully controlled studies. Hoff warned against over-enthusiastic neglect of other physical treatments and emphasized the

need for an integrated therapeutic approach to the hospitalized psychiatric patient, while Kumke made an earnest appeal not to ignore the all-important role psychotherapy plays in many psychiatric conditions.

Pierson reported four interesting observations on the effect of chlorpromazine on what he calls collective anxiety. In each instance chlorpromazine had been effective in decreasing anxiety, tension and panic in a group of people under stress, either when administered to the leader or to members of the group. Pierson thinks that his observations might point the way to new means of controlling panic in disasters, and that chlorpromazine or drugs with similar action might become useful agents in "social psychiatry".

The well-known *side-effects* and *complications* of chlorpromazine and reserpine were discussed. Interesting and unexplained is the fact that jaundice following the use of chlorpromazine is very rare in some countries, for instance, France and Germany, while it occurs in 1-2.5% of cases in other countries. A similar situation exists with regard to this complication in Texas, where it is extremely rare, and the rest of North America, where its incidence is of the above order.

Aksel reported on the cellular changes observed in the brains of rabbits and cats killed with toxic doses of chlorpromazine. He found chromatolytic changes, vacuolization and nuclear changes in nerve cells with no changes observed in the glia or the vascular system. The nerve cell changes were most pronounced in the globus pallidus, corpus striatum, cerebellum and hypothalamus.

Bleuler had observed rupture of the stomach in two patients receiving reserpine. One of the patients died. There had been no warning symptoms in these cases.

The extrapyramidal or Parkinsonian syndrome which occurs as a common side-effect of chlorpromazine, and more frequently of reserpine therapy, had been studied by several speakers. Letailleur has observed an oculogyric crisis in one of his cases. Freyhan was able to show that some of his patients who developed a particularly pronounced Parkinsonian syndrome had a positive family history of extrapyramidal disease; he thinks it possible that the occurrence of Parkinsonian symptoms in patients receiving chlorpromazine or reserpine may be related to a constitutional weakness of the extrapyramidal system. Several workers insisted that the extrapyramidal syndrome occurring with chlorpromazine and reserpine is not identical with spontaneous Parkinsonism (Fluegel), and it was reported that a careful analysis of electromyographic tracings of the tremor in both conditions brings out characteristic differences (Hoff). There seemed to be general agreement, however, that the drug-induced Parkinsonian syndromes were not permanent.

A number of interesting *physiological* observations and theories regarding the action of chlorpromazine and reserpine were presented. Decourt discussed his concept of narcobiotic action which, according to him, is the specific mode in which chlorpromazine influences cellular functions not only in the human and animals but also in the fungi and protozoa. Dell and his co-workers elaborated on their previously published evidence of an adrenergic mechanism in the reticular substance of the brain stem. Terzian, who had done the first work on the effects of chlorpromazine on the EEG, repeated Himwich's experiments on the effect of reserpine on the reticular activating substance. Himwich had found that reserpine has an excitatory effect on the reticular activating system, but Terzian was able to show that this excitatory action occurred only when the animal was exposed to sensory stimuli. If the animal was kept completely free from any stimulation, reserpine would have an inhibitory effect on the reticular activating system. Terzian speculated on the nature of this "ambivalent" action of reserpine by assuming that the cephalad and the posterior portions of the reticular system have a differential response to reserpine. Werner stated that according to his experimental evidence the inhibitory action of reserpine was dependent on the presence of the cortex, while chlorpromazine would become even more effective in the decorticate brain. Bleuler mentioned the

recent findings of Swiss research workers in Washington who had shown that the action of reserpine was associated with liberation of serotonin while no similar effect could be demonstrated with chlorpromazine. Bente has studied several thousand EEGs of persons under the effect of chlorpromazine and has noted a tendency to slowing of cerebral rhythms and a definite enhancement of previously present but possibly latent abnormalities of the EEG. Denber reported on his experiments with mescaline and chlorpromazine. He was able to block the mescaline-induced psychotic manifestations and EEG changes with chlorpromazine, which would restore the subject's mental status and the EEG to normal. Soulaire has demonstrated a synergistic action of insulin and chlorpromazine in that the hypoglycaemic action of insulin is increased when chlorpromazine is administered simultaneously although chlorpromazine alone will not produce hypoglycaemia.

Laborit, who was the first to take chlorpromazine out of the laboratory into the clinic in 1951, discussed the electrolyte shifts, that is, the movement of potassium, calcium, sodium, and magnesium in and out of the cells, which occur during chlorpromazine therapy. He also reported on a new steroid substance with anaesthetic properties which has shown great promise in the treatment of delirium tremens.

Comparatively few contributions concerned themselves with the *psychological* aspects of the new drugs. A detailed account of the dynamic sequence observed in a patient undergoing chlorpromazine sleep therapy was reported by Azima, who stressed the possibility of using these new drugs to produce a state of artificial regression beyond the previous fixations and into more primitive stages of libidinal development. Petrie *et al.* compared the psychological structure of lobotomized patients and those receiving chlorpromazine. Employing Eysenck's introversion-extroversion tests, they found that in one essential aspect, lobotomized and chlorpromazine-treated patients were reacting in opposite directions: lobotomized patients tended to be more extroverted, while patients receiving chlorpromazine were distinctly more introverted. They confirmed previous findings of other workers that chlorpromazine did not produce any significant impairment of the higher psychic functions. Lehmann discussed the rationale of chlorpromazine therapy at physiological and psychological levels, pointing out that the drug depressed the reticular activating substance, reduced the capacity for arousal reaction in the brain, and in this manner dampened the excessive excitatory processes which are engendered by emotional disturbances. He compared the effect of chlorpromazine on psychic functioning in emotionally tense patients to the defence mechanism of isolation.

In summing up, Professor Delay pointed to the fact that not one of the speakers had denied or even questioned the effectiveness of these new drugs, though many problems still remain unsolved with regard to indications and contraindications, the most effective dosage, and the length of time during which the treatment should be administered. No doubt in the next few years we will see the development of a number of new pharmacological agents with similar and possibly better therapeutic action in psychiatric conditions and fewer undesirable side-effects.

H. E. LEHMANN

CANADIAN ASSOCIATION OF RADIOLOGISTS

At the 19th Annual Meeting of the Canadian Association of Radiologists in the Hotel Vancouver, Vancouver, B.C., January 16, 17 and 18, 1956, the guest speakers will be Professor William Boyd of Toronto, Dr. Charles T. Dotter, Professor of Radiology, University of Oregon, and Dr. J. H. Woodruff from the University of California.

Dr. Boyd will give the Richards Memorial Lecture, Dr. Dotter will speak on "Millisecond Radiography", and Dr. Woodruff will discuss the "Radiological Diagnosis of Renal Tumours". The meeting will open on the morning of January 17 with an address of welcome by Dr. R. C. Burr, President, and its programme will include a paper on "Osteoid Osteoma of Ischial Tuberosity" by Dr. F. G. Stuart, Victoria, B.C., and a symposium on bone tumours, chaired by Dr. M. M. R. Hail of Toronto. The annual dinner of the Association will take place that evening. On Wednesday morning Dr. Griffiths of Edmonton will discuss "Radiology and Obstetrics"; Drs. Lott and Ivan Smith of London, Ont., will read a paper on cobalt-60 beam therapy in oesophageal cancer; and Dr. Dunbar of Montreal will discuss "Radiological Diagnosis of Upper Respiratory Obstruction in Infancy". The morning session will end with a symposium on "Benign Lesions of the Oesophagus". In the afternoon there will be a presentation of interesting cases, a paper by Dr. Dale Trout of Milwaukee on the "Inherent Infiltration of the Diagnostic X-ray Tube", a paper on "Cholesterosis of the Gallbladder: Radiologic-Pathologic Correlation" by Dr. Fitzgerald of Montreal, and a symposium on tumours of the head and neck.

SOCIETY OF NUCLEAR MEDICINE

The annual meeting of the Society of Nuclear Medicine had an attendance of 160 from 23 states and several provinces at Portland, Oregon, in June, with two full days of scientific sessions. The Society is now soliciting papers for the 1956 meeting at the Hotel Utah, Salt Lake City, on June 21 to 23. Titles and outlines of proposed papers would be welcomed by Dr. Simeon Cantril, Tumor Institute, Swedish Hospital, Seattle, by January 1.

Current officers are: President, Dr. Milo Harris, 252 Paulsen Building, Spokane; President-elect, Norman J. Holter, Ph.D., Helena, Montana; Membership, Dr. Thos. Carlile, Mason Clinic, Seattle; Secretary, Dr. R. G. Moffat, 2656 Heather Street, Vancouver 9; Treasurer, L. Labbe, Ph.D., University of Oregon, Portland, Oregon.

CORRESPONDENCE

BRITISH NATIONAL HEALTH SERVICE

To the Editor:

As a recent immigrant from Great Britain, who came to Canada to practise because of disagreements with N.H.S. principles and practices, I was naturally interested to read the letter from Dr. J. H. S. Geggie in your issue of November 1.

While I find myself in agreement with him on the majority of points (I would not otherwise be here myself), I feel that I must, in fairness to colleagues in Britain, disagree with him on certain matters.

In many ways, I am sure, the N.H.S. has proved a boon to the patient, in that it has removed the financial worry otherwise attendant upon any significant illness—a worry greater than ever in these days of expensive remedies. Admittedly hospital waiting lists are long for non-emergency problems, but this is to be considered along with the knowledge that in pre-N.H.S. days the majority of these cases would not have come to operation at all, but would have remained at home, untreated and probably unseen by a doctor. The problem here is one

of volume of cases in relation to hospital beds and medical manpower available.

Dr. Geggie also states that "drugs of known and proven value are denied to" the general practitioner. This is not the whole truth. Certain drugs (such as cortisone) are in short supply because they cost dollars, and are, or were until recently, only available on specialist recommendation, in order to make the best use of the limited quantity available. Surely no one will quarrel with that principle. Otherwise, the G.P. may prescribe what he likes, with the proviso that if he prescribes certain drugs not of proven value, or which do not differ therapeutically from the standard B.P. preparations, he may be called upon to justify the use of these drugs in view of their higher cost to the N.H.S. If he can so justify his prescribing before a committee of his fellow practitioners, all is well.

Apart from these points, I agree with Dr. Geggie that the profession in Canada should take careful note of what has happened in Britain, and should see that the same mistakes are never repeated here. Patients should be free to choose and change their doctor (as they are in Britain) and certainly the "fee for service" is, in my opinion, an essential part of any medical service which is to offer the best in medical care to the patient.

JOHN S. ETHERINGTON, M.B., B.S.

1405 Lincoln Avenue,
Winnipeg 3, Manitoba,
November 21, 1955.

PRESCRIBING

To the Editor:

Increasing embarrassment appears to be developing between druggists and physicians over the refilling of prescriptions for Schedule F drugs.

Perhaps it is timely to refresh the memory of those physicians who have forgotten some of the implications of a prescription.

By definition a prescription is a formula written by a physician to an apothecary, designating the substances to be administered to a particular patient. The length of treatment is governed by the number of pills or amount of fluid medicament supplied and the amount of the material to be taken daily. A time limit for therapy thus exists.

If recovery has proceeded according to plan the one prescription should be sufficient, although frequently an additional filling of the prescription is required. The physician should bear in mind that the prescription, if it contains a Schedule F drug, may not be refilled unless the practitioner so directs and specifies the number of times that it may be refilled. If no such direction is shown on the prescription, the druggist has two choices: he may refuse to refill the prescription, or he may take the time out to telephone the physician for a verbal approval of the refilling of the prescription. This all takes time and effort. The physician is not always readily available and undue delays and anxiety are produced.

If the druggist refills the prescription without written or verbal approval he is contravening the laws that have been enacted for the protection of the medical profession and the general public.

It behooves us, therefore, to consider when we prescribe a Schedule F drug how long the therapy should be prolonged and to specify the number of times the prescription may be safely refilled. If we do not specify that the prescription may be refilled, it may only be used for the initial filling.

J. R. MACDOUGAL, M.D.

Chief Medical Officer,
Food and Drug Directorate,
Department of National Health and Welfare,
Ottawa, Ont.,
November 9, 1955.

GENERAL PRACTICE IN AUSTRIA

To the Editor:

In Austria today it is the ambition of every young general practitioner to become registered with the Gebiets Krankenkasse (District Sick Fund), which is the largest state-operated compulsory insurance. This is understandable because 80% of the population of Austria is under one of the state medical insurances, and it is virtually impossible for the young practitioner to make a living unless he works with the insurances. However, there must be at least 400 fully insured people in the area before another doctor is allowed on the list. As the families of the insured are not counted in this estimate, it means in practice that a young man has a long wait before he gets on the Krankenkasse list.

In the Tyrol the general practitioner must spend four years in hospitals before starting on his own. For the first two years he is not paid and during the final two years he gets enough for himself but, in spite of the popular truism, it is not enough to keep a family. As seen above, most have a further period of dependence before they are able to get on with the insurances.

It is little wonder that a well-endowed wife from a rich family is the ambition of most young doctors. Fortunately the custom of large dowries has been perpetuated in Austria, but unfortunately the ability to endow a daughter properly has been negated by the fortunes of war.

Now when a doctor attains to Gebiets Krankenkasse in the Tyrol he finds that he is allowed five schillings for the first visit. This is the equivalent of 20 cents and is brought into perspective when it is realized that a large cup of coffee in a restaurant costs six schillings or 24 cents. A pound of butter costs 35 schillings or \$1.40. A gallon of gasoline costs in the neighbourhood of 60 cents. Most doctors find that their resources are strained to the utmost in order to buy and maintain a small Volkswagen. Indeed these cars cost the equivalent of \$1,600.

In the other provinces the Gebiets Krankenkasse pays the doctors on a different schedule. In each three-month period the patient is allowed one slip which he gets from his employer and takes to the doctor of his choice on the Krankenkasse list. This entitles him to get any and every treatment that he may require during this three-month period. At the end the doctor sends in all the forms that he has collected during the period. Then in full payment for each of the forms he gets 26 schillings or slightly over one dollar. There are a few cases where he may claim more than the dollar. For a minor operation he may claim less than one dollar and if he is present at a delivery he may claim less than three dollars.

After the first 600 patients he is allowed only one half dollar and after 300 more it drops even further. It is obviously uneconomic for the doctor to see too many patients. It is to the doctor's benefit to see the patient once during the period and hope that he does not need to return. The doctor is paid one dollar for the three months, whether he sees the patient once or 30 times. This leads to abuses in practice.

The average insurance doctor's income is slightly over 6,000 schillings a month. Most have 3,000 left to keep themselves and their families after taxes and expenses. The equivalent of \$120 is not very much when he has to face up to the high costs in other fields.

Faced with overcrowding within the field and poor economic conditions, most doctors are dissatisfied with their opportunities. There are not as many medical students now, but the older doctors are not retiring because their incomes were destroyed during the war, and the large crop of wartime doctors are still young.

In general the skilled tradesmen are better off and are able to build their own homes. Most young doctors despair of ever being able to build their home. Indeed with the fall in income which puts the doctor at a lower

economic level than a skilled worker, there has been a great loss of prestige.

However, one young Viennese told me that the sense of freedom now felt with the end of the Occupation did a lot to compensate him and his family. Admittedly he could not take more than two weeks off during the year but during this time he could take his car across international boundaries with ease. With the Russian Bear just a few miles to the east he hoped that it would remain this way.

JOHN VALENTINE, M.B., Ch.B., L.M.C.C.

c/o Box 25, Gingindhlovu,
Zululand, South Africa.

REPETITIO AD NAUSEAM?

To the Editor:

In today's issue of the *Montreal Daily Star*, p. 36, there is a Canadian Press release reporting what seems to have been the highlight of a meeting of District No. 4 of the Ontario Medical Association held yesterday at Hamilton, Ontario. According to the report, the president-elect of the Ontario Medical Association, Dr. J. C. C. Dawson, spoke to 200 (!) physicians, where he reportedly said among other things that the medical profession "does not hold as high a place in public esteem as it once did", and that "the profession will not regain its position in public opinion as long as there is lack of unity and harmony among doctors." It is further said that Dr. Dawson appealed to the group to make every effort to wipe out fee-splitting and other undesirable practices.

The writer of this letter, a physician who is not a fee-splitter, or a drug pedlar, or an abortionist (so help me!), agrees with Dr. Dawson that the esteem of our profession has indeed fallen comparatively low and that fee-splitting exists. Nevertheless, I venture to take issue with our confrère very strongly on two counts at least.

1. Fee-splitting, which has always existed and will exist here and there, like any other evil, will not be eradicated by preaching *ex cathedra* to the unethical man. Censure him, take away his licence, send him to the gallows, if you will—do what you can, but do not convert a meeting of the medical profession into a medical confession period, as if the transgression is characteristic of the membership at large.

It is just such frequent official and public utterances that give Messrs. Smith and Jones the wrong impression and are responsible for the fall of our esteem. It is sickening and nauseating to hear again and again the same re-hash in official medical circles which thus, as a matter of course, creates the justified impression that where there is smoke there must be fire, with the conclusion, consequently, that the fire must be greater than the smoke.

2. Yes, there is indeed also "lack of unity and harmony among doctors". This is because some of our leaders in the profession put on the admonishing garb of the prophet and saint and very unethically bask in their glory in vaudeville-like fashion at lay meetings, in the public press and in television shows. To those I say: Physician and confrère! Follow the modesty and ethics of your predecessors; mind your medical business as best you can; rid yourself of your culprits and transgressors—and our professional esteem will rise again, as of yore.

M. B. ETZIONY, M.A., M.D.

475 Champagneur Avenue,
Montreal, Que.,
October 28, 1955.

ABSTRACTS from current literature

MEDICINE

Factors in the Etiology of Constrictive Pericarditis

DETERLING, R. A. AND HUMPHREYS, G. H.:
CIRCULATION, 12: 30, 1955.

Despite the success of the surgical treatment of constrictive pericarditis, its etiology remains obscure in many cases. Although tuberculosis is frequently cited, in many reported cases a meticulous search has failed to reveal any evidence of this disease. Recent attention has been directed to a possible relationship to chest trauma, and it has been suggested that chronic constriction may result from pericarditis associated with rheumatic heart disease. In order to explore these and other factors, the records of all patients with a diagnosis of pericarditis treated at the Presbyterian Hospital in New York between 1930 and 1954 were reviewed. The number of these cases totalled 416. In this group there were 5 patients with the clinical but unproven diagnosis of chronic constrictive pericarditis, and 25 in whom the diagnosis was proved by operation or autopsy. The symptoms included dyspnoea, orthopnoea, fever, cough, and precordial pain. The physical signs included elevated venous pressure, ascites, oedema, enlarged heart, pleural effusion, cardiac murmurs, auricular fibrillation, pericardial friction rub and cyanosis. The roentgen findings included diminished cardiac activity, enlarged heart and pericardial calcification. The electrocardiographic findings included low voltage, inverted T-waves, pulse rate above 85, arrhythmias and axis deviation. Diminished pulse pressure was noted in a large percentage of cases.

Investigation of the etiological basis for constrictive pericarditis in this group, and in reports by other authors, indicates that it is impossible to determine a definite cause in many patients. Among *proved* causes, tuberculosis is the most frequent. The writers present evidence that injury, purulent infection of the pericardium and rheumatic heart disease may produce the constrictive syndrome. They emphasize the concept that the symptoms and physical signs result from a myocardial factor as well as pericardial compression. S. J. SHANE

Prednisone and Prednisolone as Therapeutic Agents.

SPIES, T. D. *et al.*: J. A. M. A., 159: 645, 1955.

Prednisone and prednisolone have been found effective in the treatment of the same conditions as those in which cortisone, hydrocortisone and pituitary corticotropin (ACTH) prove beneficial. When given systemically in sufficient amounts they have the same antirheumatic, anti-inflammatory and antiallergic effects. The same complications follow their use, except that they do not promote sodium and water retention. Per unit of weight they are four to five times as active as cortisone and hydrocortisone. The authors make special reference to the treatment of rheumatoid arthritis with these newer compounds. They emphasize that use of these drugs comprises only one aspect of the treatment of these patients. Other measures include adequate rest, nutritious diet, physiotherapy and the correction of deformities. In an attempt to keep the dosage of these drugs as low as is compatible with therapeutic efficacy they tried a combination of acetylsalicylic acid 300 mg. with prednisone 0.75 mg. and ascorbic acid 22.5 mg. This combination was given to 19 patients with active rheumatoid arthritis whose disability was enough to keep them from working but not enough to confine them to bed. Treatment consisted of two tablets four times daily. Each patient showed definite, prompt and continued clinical improvement, both subjectively and objectively. The circulating eosinophils in the peripheral blood did not change significantly. Similar studies with a tablet containing acetylsalicylic acid 300

mg. and prednisolone 0.5 mg. in the treatment of 15 additional patients produced essentially the same results. While severely affected patients will not obtain as much relief from these mixtures as they would from larger doses of corticosteroids, the combination of acetylsalicylic acid and prednisone or prednisolone does have merit in that it improves the patient's condition and boosts morale in a chronic disease and does it on a dose of corticosteroids low enough not to be likely to produce undesirable side-effects in long-term therapy. N. W. McQUAY

Circulatory Effects of Mitral Commissurotomy with Particular Reference to Selection of Patients for Surgery.

FERRER, M. I. *et al.*: CIRCULATION, 12: 7, 1955.

This paper presents a study of 60 patients referred to a clinic as suitable candidates for mitral commissurotomy. Of these 60 patients, 15 were deemed unsuitable after clinical study alone; 10 proved to have active rheumatic carditis and five subacute bacterial endocarditis. Another 15 were rejected as candidates for operation after physiological study; 11 of these had little or no resting pulmonary artery hypertension; in two there was evidence that left ventricular failure accounted for the pulmonary hypertension found, while two without disabling symptoms had only mild pulmonary hypertension and represent a phase of the problem not yet clearly defined. Thirty-one patients were considered suitable for surgery after physiological studies; of these three eventually refused commissurotomy and one was rejected because of an aneurysmal left atrium.

Of the 27 subjects who underwent surgery, eight were believed to have clinical and physiological evidence of an excellent result, while five had good results. Nine patients showed no clinical or physiological evidence of any improvement, and of these, six are now dead. The remaining five died at operation.

As a result of this study the writers would now reject eight subjects who were originally advised to undergo surgery, believing that their predominant difficulty was myocardial insufficiency and not valvular disease.

Their experience with the combined lesions of mitral stenosis and insufficiency is somewhat limited but is discouraging. Indeed they have learned from the five patients in this series with a double mitral murmur that one cannot expect a successful commissurotomy when the murmur of mitral insufficiency coexists with a heavily calcified valve.

These workers believe that clinical criteria appear as yet inadequate for the selection of the proper candidate for mitral commissurotomy, as there is no good clinical means of establishing in every instance the presence of pulmonary hypertension, which remains the best evidence of a significant degree of mitral block.

They consider that objective physiological measurements represent the best criteria for the effects of surgery; subjective impressions may be unreliable. S. J. SHANE

The Electrocardiographic Diagnosis of Acute Myocardial Ischemia.

MYERS, G. B. AND TALMERS, F. N.: ANN. INT. MED., 43: 361, 1955.

Both the Levy (anoxia) and the Master (exercise) tests have been used extensively for the induction of electrocardiographic changes in the objective diagnosis of myocardial ischemia. The latter method is preferred in most clinics. It is employed for diagnostic purposes when there is a suspicion but no clear-cut evidence of coronary insufficiency; and it is utilized for prognostic purposes in asymptomatic, ambulatory patients after recovery from myocardial infarction, to evaluate tolerance of prescribed activity.

In both the Levy and the Master tests, displacement of the ST segment is the critical feature on which an

objective diagnosis of coronary insufficiency is based. The writers feel, therefore, that it is of great importance that spontaneous ST displacements (that is, those not caused by the test) should be carefully evaluated to minimize errors in interpretation of these diagnostic tests.

They illustrate several electrocardiograms in which spontaneous ST displacements occurred which, had they been ignored, would have led to an erroneous diagnosis of coronary insufficiency on performance of one or other of these two tests. Among the spontaneous ST changes that they describe are included the pseudo-depression associated with tachycardia and the exaggeration of the T_p wave having the same etiology. They stress that these are to be carefully distinguished from abnormal depression secondary to acute subendocardial injury. In the former, the ST segment displays a continuous ascent in a curve with upward concavity; in the latter it exhibits a characteristic horizontal or sagging depression of 1 mm. or more in the absence of cardiac glycosides.

Changes in the ST segment of the resting electrocardiogram that might have formed the basis for the prediction of abnormal tests are emphasized.

They indicate that abnormal ST displacements are much more frequent in leads V₁ and V₂ facing the anterior or anterolateral aspect of the apex. Electrocardiographic evidence localized to the right precordial leads is considered by them to be associated with septal ischaemia; evidence localized to the back leads or to aVF or both is considered to be associated with posterior ischaemia.

The authors stress that the standard limb leads are not positive as frequently as are the chest leads, and that they have shown no abnormalities that are not better evaluated by multiple chest leads.

It appears, therefore, that both the Master and the Levy tests should be carefully planned, and even more carefully interpreted. S. J. SHANE

Treatment of Coronary Thrombosis with Myocardial Infarction.

WOOD, J. E., BECKWITH, J. R. AND CAMP, J. L.
III: J. A. M. A., 159: 635, 1955.

In the evaluation of therapy for patients with acute myocardial infarction some estimation of the severity of the infarction must be kept in mind. Several authors have attempted to divide their patients into poor-risk and good-risk categories within two to three days after infarction. Poor-risk patients have been found to have one or more of the following conditions: history of a previous infarction; presence of intractable pain; severe continuing shock; presence of congestive heart failure; occurrence of an arrhythmia; history or presence of thromboembolic phenomena; and a greatly enlarged heart. The good-risk patient did not have these conditions and in this group a mortality of 3.4% and a thromboembolic incidence of 1.3% were found as contrasted with a mortality of 60% and a thromboembolic incidence of 11.5% in the poor-risk group. Therapy included such general measures as relief of pain (morphine preferred with atropine as an adjunct, if necessary); oxygen for dyspnoea, cyanosis, shock, or poor pain control; liquid diet in the first few days followed by low-salt, low-calorie diet; liquids may be given up to 3,000 c.c. daily and should not be iced; attention to the bowels with the use of a bedside commode. Chair and bed rest beginning on the second day was favoured by the authors over strict bed rest and has not been attended by any increase in mortality in either good-risk or poor-risk patients. Studies have shown that less cardiac work is done in the sitting position. The presence of shock is associated with an increased mortality and suggested therapy for this complication included morphine and oxygen for pain; atropine for bradycardia; plasma or blood transfusion for collapsed veins; digitalis for congestion; correction of arrhythmia with quinidine; and arterenol by intravenous drip. Anticoagulant therapy may not affect the incidence of mortality but does reduce the incidence of thrombo-

embolic phenomena. Phenindione (Hedulin and Danilone) was favoured over bishydroxycoumarin (Dicoumarol) because of its ability to reduce prothrombin time in one or two days and yet allow more rapid return to normal in the event of haemorrhage. Treatment with anticoagulants must be watched closely in patients with liver disease or liver congestion, renal insufficiency, and those in the older age groups. Anticoagulants should be avoided in patients with a bleeding tendency, peptic ulcer, tumours of the gastro-intestinal or genito-urinary tract and vitamin K deficiency. Digitalis was used for congestive heart failure although a few cases with mild congestion may be controlled by one or two injections of a mercurial diuretic. In the treatment of arrhythmias the routine use of quinidine is not advisable. It should be reserved for ventricular premature contractions, ventricular tachycardia and paroxysmal tachycardia. In the treatment of auricular flutter and fibrillation digitalization should precede quinidine. N. W. McQUAY

SURGERY

Observations on the Surgical Physiology of the Human Liver Pertinent to Radical Partial Hepatectomy for Neoplasm.

BRUNSCHWIG, A.: CANCER, 8: 459, 1955.

It has been demonstrated that in the cat, dog and rabbit, resection of up to three-quarters of the liver could be survived and that in 36 days repair is so extensive that the original weight of the organ is regained. The author gives case histories of patients on whom partial hepatectomy had been performed to show that this is also probably true of the human liver, but that regeneration does not occur until a physiological demand is created. The removal of a large mass of neoplasm-containing liver is not as disturbing as the removal of functioning tissue. The gradual removal of liver tissue may result in the shifting of the physiological load to uninvolved parenchyma without hyperplasia. The control of bleeding in normal and cirrhotic liver and effects of occluding the portal vein and/or the hepatic artery are described. BURNS PLEWES

Investigations Into Thymic Disease and Tumour Formation.

KEYNES, G.: BRIT. J. SURG., 42: 449, 1955.

The relationship of the thymus gland and myasthenia gravis and the results of thymectomy have been widely discussed, but there is an especially difficult aspect—thymomata. Thymus tumour occurred in 41 of the 260 patients with myasthenia gravis seen by the author and there have been an additional few in patients with no symptoms. Though a variety of thymic tumours have been reported, and few are described as malignant, all thymomas are in a sense malignant, for they provoke a dense fibrous capsule, become adherent to surrounding structures, and recur, and secondary tumours sometimes form. Lymph node and distant metastases are rare.

The diagnosis of a thymoma should be entertained when myasthenia gravis develops very rapidly or is unusually resistant to control by prostigmine. Careful radiography can usually demonstrate the mediastinal tumour. High voltage irradiation renders many tumours resectable.

The complex disease associated with thymic tumour and the expert team developed to treat it are thoroughly discussed. BURNS PLEWES

The Gastro-oesophageal "Sphincter" and the Mechanism of Regurgitation.

MARCHAND, P.: BRIT. J. SURG., 42: 504, 1955.

The mechanism of vomiting and regurgitation of stomach contents into the oesophagus was studied in living and

autopsy subjects by x-ray examinations and tubes. An important factor was increased intraperitoneal and intra-gastric pressure. Reflux is prevented by the angle at which the oesophagus enters the stomach, oesophageal peristalsis, the tone of lower oesophageal musculature, posture and the low intra-abdominal pressure. Clinical regurgitation was found to be influenced by the following factors: change in posture, gastric distension, diminished peritoneal capacity, swallowing, and loss of the normal gastro-oesophageal angle. Heartburn follows irritation of the oesophagus by gastric reflux and if this is persistent and prolonged the symptoms of oesophagitis occur. (This essay won the Moynihan Prize in 1954.)

BURNS PLEWES

Traffic Injuries — A Surgical Problem

ZOLLINGER, R. W.: A.M.A. ARCH. SURG., 70: 694, 1955.

An examination of the attendance at the Emergency Department of Mt. Carmel Hospital, a 400-bed institution in Columbus, Ohio, showed that of 9,050 visits in 1953, 724 were for traffic injuries. About 1 in 4 traffic victims required admission and 71% came in between noon and midnight. It is shown that the hours of dusk and darkness are the most dangerous for travel and that fatigue is a factor. Sixty-five per cent of deaths and 60% of traffic injuries were in persons under 30 years of age.

Emphasis is placed on the instruction and experience of nurses in the emergency department, for interns do not remain there very long. The head is the most commonly injured part of the body, and most lacerations must be cared for with attention to the cosmetic result. A quarter of the cases admitted required shock therapy in the Emergency Department. Only a small percentage of the emergency visitors required specialized medical personnel.

There were 30 deaths; 13 patients were dead on arrival and 8 died in the Emergency Department. Although abdominal injuries were infrequent, they were a major cause of death among those who died after being admitted to hospital.

BURNS PLEWES

OBSTETRICS AND GYNÆCOLOGY

Management of the Pregnant Diabetic.

PEEL, J. H.: BRIT. M. J., 2: 870, 1955.

The clinical association of diabetes mellitus and pregnancy is still comparatively uncommon, though increasing. The obstetrical interest lies in relation to problems of fetal size, placental function, intrauterine and neonatal death, hydramnios, toxæmia and congenital abnormalities in general. The over-all fetal mortality remains high.

Three groups of cases are briefly discussed: (a) the pre-diabetic; (b) the person developing diabetes during or soon after pregnancy; (c) the established diabetic. The indications for therapeutic termination are considered. The main problems during the antenatal period arise during the last trimester, when there is a special tendency for the development of hydramnios and toxæmia, and for intrauterine death to occur. The high fetal loss is considered in relation to severity, age of onset and duration of diabetes, and to hydramnios and toxæmia.

The results of a clinical trial using oral hormones (stilboestrol and ethisterone) are given, suggesting that they have no effect upon fetal survival.

Brief reference is given to hormone assays which have been carried out at King's College Hospital, London, and their possible significance is indicated.

Premature termination of pregnancy before the end of the 37th week is recommended, and the relative places of Cæsarean section and induction of labour are discussed.

The importance of hyaline membrane disease as a cause of neonatal death and its possible relation to intra-uterine anoxia are explained.

ROSS MITCHELL

THERAPEUTICS

Long-Acting Coronary Vasodilator Drugs: Metamine, Paveril, Nitroglyn and Peritrate.

RUSSEK, H. I. ET AL.: CIRCULATION, 12: 169, 1955.

Evaluation of vasodilator drugs in the treatment of angina pectoris continues to present a difficult problem because of the lack of objective methods of study, the element of subconscious bias on the part of both patient and physician, and the unreliability of pain as a quantitative measure of underlying coronary insufficiency. It has been shown, however, that the ability of vasodilators to modify the electrocardiographic response to standard exercise (Master two-step test) in carefully selected patients provides a sound basis for assessing the relative and absolute value of each of such agents in the treatment of this disorder.

Employing this technique, a study of Paveril (dioxylene phosphate), Metamine (triethanolamine trinitrate bi-phosphate), Nitroglyn (coated granules of nitroglycerin) and Peritrate (pentaerythritol tetranitrate) was undertaken in 21 patients in whom control records obtained after standard exercise remained relatively constant from day to day. The results obtained with Metamine, Paveril and Nitroglyn were in sharp contrast with those observed after the administration of Peritrate. They may be summarized as follows:

1. Metamine produced little or no significant effect on exercise response as measured electrocardiographically in all patients in the series.

2. Paveril in some instances was mildly effective, but its action was not sustained and its influence was never striking even with massive dosage. Only 6 of 21 patients showed significant improvement in exercise response following the use of this drug. Paveril does not appear to be as potent as papaverine in comparable dosage.

3. Nitroglyn, in spite of the logic behind its use, gave disappointing results. In the usual recommended dosage, 2.4 mg. (1/25 grain), the preparation appeared totally inert. With larger doses, 4.8 to 9.6 mg. (2/25 to 4/25 grain), Nitroglyn evoked slight to moderate improvement in exercise response for a period of six hours following its administration in almost two-thirds of the patients tested. Nevertheless, the drug failed to induce a normal electrocardiographic response to exercise in any of the 21 patients in the series, a result far surpassed by the sublingual administration of nitroglycerin and by Peritrate, respectively.

4. Peritrate, in a dose of 10 to 20 mg., showed a marked modifying influence on the response to standard exercise in 14 of the 21 patients tested. The effect of this agent was comparable to that of nitroglycerin, but its action, after a latent period of 60 to 90 minutes, could be demonstrated as long as five to six hours after the administration of a therapeutic dose. Clinical response was markedly attenuated or totally abolished, however, when Peritrate was taken after food. Of the four drugs tested only this agent appears worthy of the designation "long-acting coronary vasodilator." Peritrate appears to satisfy the need for prolonged coronary vasodilatation in most patients with angina pectoris.

S. J. SHANE

INDUSTRIAL MEDICINE

Emergencies in General Practice. Agricultural Pesticides.

EDSON, E. F.: BRIT. M. J., 1: 841, 1955.

Pesticidal chemicals form a large group. Information regarding emergencies, which can arise from their use, is presented for the benefit of general practitioners, especially those located in areas of intensive agriculture.

Occupational hazard is limited mainly to spray operators, scientific workers and workers in such places as

farm, orchard, greenhouse, and seed dressing establishments. The main risks are those of skin contamination and inhalation. Ingestion may occur; this may be deliberate or accidental.

General procedures for medical emergencies are suggested. With chemicals of low toxicity, emergencies are rare. Attention is focused on dinitrocresol and organic phosphorus compounds with reference to mode of action, clinical picture, laboratory tests and treatment. The author then presents the less widely used arsenical, organic mercurial, and nicotine compounds. In connection with dinitrocresol poisoning it is suggested that all hospitals in the major cereal-growing areas should be equipped to determine blood dinitrocresol levels very quickly. As there is no known specific antagonist to the effects in the body, treatment is aimed at the rapid promotion of maximum heat loss and the complete relief of anoxia, restlessness, and dehydration. In acute cases there should be no exposure to dinitrocresol or other hazardous chemicals for at least two months. This usually means until the next season.

All present-day organic phosphorus insecticides cause similar toxic effects, by inactivating acetylcholinesterase enzyme (ChE) of the tissues and thus permitting acetylcholine to accumulate dangerously. The clinical diagnosis of organic phosphorus poisoning relies on concurrent effects on secretions, muscles and brain. There are no external indications of contamination, but there will be a history of exposure within the previous few days. The confirmation of diagnosis relies on demonstrating reduced ChE activity in the circulating blood.

The safeguarding of workers in these modern agricultural operations is a matter of great concern in which the practitioner can play an important role. It consists not only in medical treatment, but also in emphasizing the need for care on the part of the user, in detecting unsafe working methods and in carrying out periodic scrutiny of workers during their season of major risks.

An appendix gives details of the technique for blood dinitrocresol and blood cholinesterase estimations.

MARGARET H. WILTON

Occupational Aspects of Rheumatic Diseases.

MINTZ, B. AND GOLDWATER, L. J.: *INDUST. MED.*, 23: 335, 1954.

Rheumatic diseases constitute a significant morbidity problem with important economic implications from the point of view of loss of productivity and wages. Most affected individuals can continue to work although the more severely disabled may require adjustments either by changing their job or their way of working. Conditions associated with an excessive incidence of arthritis and rheumatism include outdoor work and exposure to cold, sudden temperature changes, and wet; heavy work, excessive use of the same muscles, postural conditions involving strain on the musculo-skeletal system, and acute trauma.

These findings resulted from an extensive review of existing information on the prevalence of the rheumatic diseases in industry and their possible association with specific conditions. Knowledge of the contributing occupational factors provides a key to prevention. The investigations studied included both English and American; the data for analysis had been derived from many sources—plant medical records, studies of absenteeism, individual case histories, compensation reports, rehabilitation experiences, surveys of disability in industrial and other population groups, and physiological investigations.

A brief historical survey indicates the apparent relation between occupation and "rheumatism" reported in the literature since the early part of the century. Considerable detail is also given regarding the prevalence of rheumatic diseases in industry as revealed by recent studies. For example, among New Jersey's 40,735 compensated claims covering the period from

January 1949 to July 1951, 6% were due to diseases of the bones and organs of movement.

In a number of surveys occupational associations were suggested. The association of rheumatism with agricultural labour and domestic work has been noted, also the frequency of occurrence among miners and among certain workers in the iron and steel industry such as blast-furnace men. Reference is made also to two occupational diseases which have been associated with arthritic lesions: caisson disease and silicosis. The literature also yielded information suggesting the implication of various factors including heavy lifting, strain on the musculo-skeletal system and acute trauma.

The authors stress the limitations of the available data and the tentative nature of the evidence. Association does not necessarily imply a relationship. Nevertheless they consider its importance in providing guides in the vocational placement of the arthritic worker.

MARGARET H. WILTON

PROVINCIAL NEWS

BRITISH COLUMBIA

The Annual Meeting of the Canadian Medical Association, B.C. Division, took place in the Hotel Vancouver, October 4 to 7, and had a large attendance of members from all over the Province. The total registration was over 400.

The first day was taken up with a General Assembly meeting, and in the evening the College of Physicians and Surgeons held its Annual Meeting. Honorary life memberships in the College were bestowed on Drs. George E. Darby, Arthur L. Crease, Stanley Paulin, and Gordon Burke.

Dr. T. L. Fisher of the Canadian Medical Protective Association gave an address entitled "Why Malpractice Suits?". His address excited much discussion, and was most instructive and helpful.

A remarkably good clinical programme was part of this Annual Meeting, covering three days and including round table discussions in medicine and surgery. Ample provision was made for recreation, especially golf and fishing, and a most successful dinner dance was held on *H.M.C.S. Discovery*. The proceedings closed with a banquet at the Hotel Vancouver, where Peter Larkin, Ph.D., Chairman of the International Commission on Fisheries, was the guest speaker. A feature of the meeting was the increasingly popular hobby show.

Visiting ladies were well provided for, in the way of entertainment, by a committee under the chairmanship of Mrs. Frank A. Turnbull.

A special drug treatment centre for selected groups of addicts is to be established at Oakalla prison. First steps towards this have been taken with the calling for applications for three specialist staff positions: a social worker, a probation officer and a teacher. Other appointments are to be made.

The Victorian Order of Nurses through its Nanaimo branch has rendered such good service in that city that a service club (Altrusa Club) has launched a campaign to collect \$4,000 to finance the work for a third year. There is one nurse on duty at present, and a relief nurse is needed.

Campbell River was visited by mobile x-ray buses in November, when free chest radiographs were available to all.

The King's Daughters Hospital at Duncan is to be completely rebuilt, and for a start a new unit will be constructed as the core of the new institution. The present hospital is regarded as quite inadequate for the needs of the area it serves. It is "aging and outmoded", in the words of Sir Philip Livingston, F.R.C.S., chairman of the hospital board's sub-committee. It is 44 years old.

Dr. George F. Elliot, assistant provincial medical health officer, has given a report on the administration of Salk vaccine in the province so far. His report is most encouraging. None of the five-, six- or seven-year olds who received the three doses in May and June has had the infection, whereas there were 15 cases in the children 4 to 8 years old not given vaccine.

There have been no untoward episodes in connection with administration of the vaccine, which was all prepared in the Connaught Medical Research Laboratories in Toronto.

Finance Minister James Sinclair, who was injured in a fall in Russia, has been recuperating in a Vancouver hospital. He had developed jaundice, and was a sick man when he reached the Coast, but is recovering nicely now and has left for his home in Ottawa.

There has been a fair amount of influenza in the province for the past month, as is usual at this time of the year; in one town, Bralorne, there has been a fairly severe epidemic, closing the schools, postponing public gatherings, and swamping the medical and hospital facilities. There have been no deaths.

Dr. Harold Robinson, well-known internist of Vancouver, has been appointed Medical Director of the Canadian Arthritis and Rheumatism Society.

A three-day refresher course was held in St. Paul's Hospital, Vancouver from October 27 to 29 inclusive. This is the first such course given by St. Paul's, and was a most successful affair. The new auditorium was used, and it is admirably fitted for such work, being large, well-lighted and equipped with a public address system.

Dr. Martin L. Hoffman, well-known internist and lecturer of Montreal, was the guest speaker, and was outstanding as a lecturer. The medical staff of St. Paul's provided speakers whose addresses and lectures were of a very high standard of excellence. The emphasis of the meeting was on general practice, and there were over 110 registrations, men coming from all parts of the province. It is hoped that this will become an annual affair.

J. H. MACDERMOT

SASKATCHEWAN

The Saskatchewan Division of the Canadian Mental Health Association, claiming that overcrowding is still a serious problem in the province's mental hospitals, presented a brief to the Provincial Cabinet, recommending that 300-bed hospitals be built at Prince Albert, Saskatoon, Yorkton and Swift Current.

The Association recommended that:

1. The existing mental hospitals at North Battleford and Weyburn be limited to 1,000 beds or less.
2. The new hospitals be functionally sound, according to modern psychiatric architectural practice.
3. Greater emphasis be placed on the provision of accommodation which will meet the average standard of community living.
4. Additional space be provided for recreational and occupational activities.
5. Elderly patients in mental hospitals be cared for on one floor, preferably the ground floor.

6. There be liaison between the nursing homes under the Department of Social Welfare and the mental hospitals so that psychiatric care may be given to those who need it, and nursing home care given to those who have recovered from their illness.

The Association said that overcrowding in mental hospitals in Saskatchewan is now so general that space must be doubled to provide adequate accommodation for the present patient population.

A compulsory medical care plan proposed for the Assiniboia-Gravelbourg Health Region has been turned down. The latest release would indicate a vote of 7,280 against and 1,305 for.

Conceived some 10 years ago by the C.C.F. government, the plan, which has been operating since 1946 for residents of the Swift Current Health Region, was also defeated in the Regina Rural Region.

The *Regina Leader Post*, under date of November 15, 1955, carried the following note:

"While all the 87 polls where votes were cast on November 3 had not been reported, the last count stood at 13,600 against the plan, compared with 4,407 in favour. There are still 23 polls to report and it is expected they will make little difference in the final outcome, as they are small polls, made up of two villages and parts of three municipalities."

The Medical Audit Bureau sought by the Sister Superior of the Notre Dame Hospital, North Battleford, and several of the doctors, was recently announced in a statement by the Advisory Board of the Notre Dame Hospital, issued with the sanction of Dr. Lucius W. Johnson, the Medical Auditor. The statement issued is as follows:

"The medical audit of the Notre Dame Hospital has been arranged by the Provincial Health Department as a means of adjusting the controversy there.

"The Department has gone to great lengths to assure complete fairness to all concerned. A committee has been formed to supervise the audit, consisting of Dr. C. L. Tisdale, representing the College of Physicians and Surgeons of Saskatchewan and the Saskatchewan Division of the C.M.A.; Dr. A. E. Brown, representing the University of Saskatchewan, College of Medicine; Mr. E. V. Walshaw, representing the Saskatchewan Hospital Association; Dr. Milton I. Roemer, representing the Department of Public Health of Saskatchewan, and Dr. Lucius W. Johnson, the Medical Auditor.

"The medical audit is a means of estimating the quality of the professional services of a hospital. Everything in the hospital that may affect the welfare of the patient is studied. The auditor searches for weakness in the service to patients and suggests remedies for them. As such it represents an effort by those concerned and by the hospital group to improve the service to the patients.

"The auditor has more than 50 years of work in hospitals as a surgeon, administrator and auditor. As a representative of the American College of Physicians and Surgeons, he audited more than 300 hospitals and participated in the College's programme of hospital standardization. Since leaving the College he has been doing medical audits in many parts of the United States. His home is in San Diego, California. The Health Department thought that it was important to employ someone who had no local affiliations," the statement concluded.

The physicians of Saskatchewan have good reason to be proud of their success in the fight against tuberculosis.

According to data compiled by the Health and Welfare Division of the Dominion Bureau of Statistics, deaths caused by tuberculosis in this province totalled 42 in 1954. This represents a death rate of 4.8 per 100,000 population, the lowest rate on record for any one of the 10 provinces, where the rates varied from a high of 26.4 to Saskatchewan's 4.8 with an average across the country of 10.3.

The Saskatchewan Government Air Ambulance Service completed 84 of a possible 85 patient flight requests during September, 39 being handled by the Regina base personnel and 45 by staff members stationed at Saskatoon.

In addition to the Regina and Saskatoon base flights, another 30 patients were transported in northern areas of Saskatchewan by companies other than the Air Ambulance, which has no facilities in the north.

Introduction of a specialized dental service for physically handicapped children at the Saskatoon Physical Restoration Centre has been announced by the Honourable T. J. Bentley, Minister of Public Health. Mr. Bentley also intimated that a similar appointment may be made in the near future for the Regina centre, which serves the southern portion of the province.

Mr. Bentley stated that such specialized treatment, requiring a team approach, is of recent origin, having been developed in the U.S.A. at several outstanding dental schools as the answer to the problem of dental care for handicapped children.

G. W. PEACOCK

MANITOBA ANNUAL MEETING

Blessed with good weather, the Manitoba Medical Association (Canadian Medical Association, Manitoba Division) held its annual meeting in the Fort Garry Hotel, Winnipeg, October 24-27, with Dr. Ruvin Lyons as acting President.

The guest speakers who contributed much to the success of the occasion were Dr. John C. Beck, Montreal; Dr. E. H. Botterell, Toronto; Dr. J. N. B. Crawford, Ottawa; Dr. Donald W. Hastings, University of Minnesota; Dr. A. D. Kelly, General Secretary, Canadian Medical Association; Dr. H. H. Saunderson, President, University of Manitoba; Dr. M. M. Wintrobe (Man. '30), Professor of Medicine, University of Utah.

The Manitoba Health Officers had a one-day session on October 24 and on that day the President's dinner for the retiring executive was held. The General Practitioners Association of Manitoba met for dinner on the 25th and elected Dr. J. F. Edwards as president. The internists, psychiatrists, surgeons and the classes of '14 and of '30 all held dinners that evening.

There was a good display of commercial exhibits which attracted much attention, and the Manitoba doctors' hobby exhibit showed their skill in other fields.

The meeting was rounded off with a reception, dinner and dance on October 27. Dr. Ruvin Lyons was elected president; Dr. J. E. Hudson, Hamiota, vice-president; Dr. C. B. Schoemperlen, 2nd vice-president; Dr. J. C. Rennie, Portage la Prairie, honorary secretary; Dr. W. J. Boyd, Winnipeg, honorary treasurer; Dr. K. J. Johnson, Pine Falls, rural member of the executive at large; Dr. F. H. Smith, Winnipeg member at large. Dr. W. A. Bigelow, Brandon, was named senior member for Manitoba for 1956.

Winnipeg was privileged to play host to the medical administrators and directors of Trans-Canada Medical Plans on November 2, 3, 4 and 5. The visitors were Drs. G. B. Shaw, Halifax; J. A. McMillan, Charlottetown, representing Maritime Medical Care; W. B. Stiver, Physicians' Services Inc., Toronto; W. E. Hume, Windsor Medical Services; J. G. McLeod, Regina; J. C. Dundee, Saskatoon; S. M. Schmaltz, Edmonton; G. L. Watson, Vancouver; Mr. Moffatt, Regina; Mr. Cronin, Saskatoon; Mr. C. Howard Shillington, Director, Trans-Canada Medical Plans; and Dr. J. L. Rochefort, Quebec Hospital Service Association, Montreal. Dr. Watson was elected President of Trans-Canada Medical Plans. Dr. P. H. T. Thorlakson, chairman of Manitoba Medical Service, presided at a dinner in the Manitoba Club for the visiting

directors, the members of the Manitoba Medical Service Board and officers, and other guests, who included Dr. Morley Elliott, Deputy Minister of Health and Public Welfare for Manitoba.

ROSS MITCHELL

ONTARIO

At the instigation of the Parents' Action League, the Ontario Government has announced that it will sponsor an inquiry by a three-man commission into the possibility of establishing a clinic at the Ontario Hospital on Queen St. West, Toronto, to treat sex deviates. The inquiry will be made by Health Minister Phillips, Dr. Kenneth Gray, assistant professor of psychiatry, University of Toronto, and Dr. F. H. Van Nostrand, director of neurology and psychiatry for the Reform Institutions Department. Attorney-General Roberts stated that there were 375 cases of sex crimes in the province last year; of these 95 occurred in York County.

Dr. Bruce Charles has been appointed chief of the Department of Medicine, and Dr. R. A. Chapin head of the Department of Anaesthesia at the Toronto East General Hospital. This hospital is campaigning to raise \$3,113,000 for expansion. Admissions number 55 a day, and more than twice every hour for every 24 hours a day an accident case goes to this hospital.

Lyndhurst Lodge, Toronto, has opened a new \$150,000 wing to make 24 more beds available for patients. Ten years ago the lodge came into existence as a centre to which war veterans who had been paralyzed by injuries were brought for rehabilitation and treatment. Five years later its work among such cases was largely finished, and it was taken over by the Canadian Paraplegic Association to continue the work among civilians.

LILLIAN A. CHASE

Dr. R. D. Defries has been awarded the Lasker Foundation Award for public health administration. This award was made to Dr. Defries at the meeting of the American Public Health Association in Kansas City on November 17. Dr. Defries is the first Canadian to win the award which is, in this case, mainly for his work in connection with the poliomyelitis vaccine programme in Canada. It is an index of the value of the award that seven of the previous eight winners have subsequently received a Nobel Prize.

Plans for a public appeal to finance completion of Toronto East General Hospital's long-range building programme have been announced. An appeal for \$3,113,000 for the building fund will be publicly launched next February; this is the first general appeal since the original hospital was built 26 years ago. It is hoped to increase bed capacity from 500 to 750 beds and to provide more accommodation for interns and nurses. The maternity department, operating suites, outpatient department and x-ray department are also to be expanded. One interesting feature of the project is that all this expansion was foreseen and included in the original master plan developed years ago. It is therefore a question of adding to, rather than replacing, the present buildings.

QUEBEC

A great number of our colleagues from across Canada enjoyed the unique charms of Quebec City during the week of October 16, by attending a series of meetings. The National Research Council led off by holding the 20th meeting of the Advisory Committee on Medical Research, under the chairmanship of Dr. J. B. Collip, on October 18 in the Medical Building of Laval University. I understand that this was the first time that this committee has met outside of Ottawa. On Wednesday, October 19, the Dean of Medicine of Laval

*"She was often depressed,
dissatisfied and unhappy . . .*

DEXAMYL* has been of remarkable value for this patient . . ."



*(This unposed photograph
was taken during the patient's interview
with her physician. The statement in quotes is from his case report.)*

'DEXAMYL' Tablets • Spansule* Capsules

Each 'Dexamyl' Tablet contains:

Dexedrine* (dextro-amphetamine sulfate, S.K.F.) . . . 5 mg.

Amobarbital ½ gr.

also available: 'Dexamyl Spansule' (No. 1) Capsules, containing the equivalent of *two* tablets
'Dexamyl Spansule' (No. 2) Capsules, containing the equivalent of *three* tablets

SMITH KLINE & FRENCH • Montreal 9

511

*Reg. Can. T.M. Off.

University, Dr. Jean-Baptiste Jobin, was host to the Association of the Deans of the Medical Schools of Canada at their annual meeting. On Thursday, October 20, the Clinical Investigation Travel Club held a one-day scientific meeting. Dr. Carlton Auger is to be congratulated on the excellent arrangements for this meeting as well as for the splendid dinner held at Le Cercle Universitaire that same evening.

The highlight of the week, obviously, was the annual meeting of the Royal College of Physicians and Surgeons of Canada, on October 21 and 22 at the Château Frontenac. As is customary, and as we have come to expect, the calibre of the scientific programme was excellent. The Lecture in Medicine at this year's meeting was given by Dr. Ronald V. Christie, professor of medicine at McGill University, who spoke on dyspnoea, while the Lecture on Surgery was given by Dr. Harold B. Atlee, professor of obstetrics and gynaecology, Dalhousie University, who spoke on "Surgery in Cancer of the Cervix".

On Sunday, October 30, the Director General of Treatment Services, Department of Veterans' Affairs, the late Dr. W. P. Warner, met at the Château Frontenac with his advisers and chiefs of services, including the senior treatment medical officers, from all D.V.A. Hospitals across Canada.

The Faculty of Medicine of McGill University has announced some faculty changes. As previously reported, Dr. Donald V. Christie assumed the chairmanship of the Department of Medicine on October 1. He has also become the physician-in-chief of the Royal Victoria Hospital and director of the university clinics at this hospital. In addition, Dr. Philip Hill has been named associate professor of medicine on a "geographical full-time basis". Three others have also been appointed to the rank of associate professor in the Department of Medicine, namely, Dr. David W. Bates of London, England, and Drs. John G. Howlett and Martin M. Hoffman of Montreal. Dr. Hill, in addition to his teaching and administrative responsibilities, will continue to do consulting work at the Royal Victoria Hospital. Dr. Bates, who is now first assistant in the Professorial Medical Unit and senior lecturer in medicine at the University of London, will join the department next year. Dr. Howlett will continue in his private practice, while Dr. Hoffman will continue as physician-in-chief at the Jewish General Hospital.

The University of Montreal, Faculty of Medicine, has announced the appointment of Dr. Jean Grignon and Dr. Bernard Baillargeon as associate professors in the Department of Medicine, and Dr. Roland Cloutier

as associate professor in the Department of Ophthalmology. All three are on the medical staff of the Hôpital Notre-Dame.

A. H. NEUFELD

NOVA SCOTIA

Dr. Roy Moreash of Berwick and Dr. J. Merritt of Halifax attended the Twentieth Annual Congress of the International College of Surgeons at Philadelphia in September and were honoured by being made Fellows.

Dr. G. W. Bethune gave a paper on the treatment of far-advanced and metastatic mammary cancer at the September meeting of the International College of Surgeons in Philadelphia.

The American College of Chest Physicians has asked Dr. Charles A. Gordon of Halifax to serve on the Committee of Physiologic Therapy. This is a privileged group responsible to the College.

The 29th Annual Dalhousie Refresher Course was held in October. Some 229 physicians registered. The weather was excellent and the social activities thoroughly enjoyed. Professor E. G. D. Murray of McGill gave the John Stewart Memorial Lecture on "Determinant Variability in Bacterial Infections". The name of Professor Murray will be long remembered in the list of fine memorial lecturers.

The Children's Hospital, Halifax, is asking for \$200,000 in their present capital campaign. This amount is necessary in order to meet financial obligations incurred by hospital improvements. These improvements include a new wing with modern operating theatres and other facilities.

Construction has commenced on the new wing of the Grace Maternity Hospital. This addition will provide 30 fine new beds and other facilities. The three-storey wing will have modern delivery rooms.

BCG inoculations against tuberculosis have been inaugurated in the Halifax city schools. High-school boys and girls are the ones who will receive the inoculations. This preventive health measure is being carried out under the direction of Dr. C. J. W. Beckwith. It is anticipated that nearly all children of the older age group will avail themselves of this opportunity to protect themselves against tuberculosis.

WALTER K. HOUSE



WHEN EVERY SECOND COUNTS!

INTRADEx
TRADE MARK

blood volume restorer

6% solution of Dextran in normal saline. Also in 'salt-free' forms.

Can be given immediately. No cross-matching. No incompatibility.
Helps to conserve the Nation's blood supplies.

GLAXO (CANADA) LTD., 36 DUNCAN STREET, TORONTO, ONTARIO



BOOK REVIEWS

STUDIES ON FERTILITY

Including papers read at the Conference of the Society for the Study of Fertility, London, 1954. Volume VI of the Proceedings of the Society. Edited by R. G. Harrison, Derby Professor of Anatomy, University of Liverpool. 151 pp. Illust. \$5.00. Charles C Thomas, Springfield, Illinois; The Ryerson Press, Toronto, 1954.

This book presents six papers by gynaecologists, eight papers on animal experimentation, and one article by a psychiatrist.

Shotton points out that pregnancy in the infertile primigravida has the same risk of abortion, ectopic pregnancy, and neonatal death as in her fertile sister. In view of the older age group there is a greater tendency to Caesarean section to avoid undue risk to the fetus. McDonald and Harrison discuss the histology of the rat testis on exposure to low temperatures. An ischaemia occurs which causes an arrest of spermiogenesis and, if the temperature is not too low, regeneration occurs in 28 days. The authors stress the danger of hypothermia of the testis during surgery.

An unusual article is written by Lowenstein on the mechanotherapy of impotence. He describes a splint-like support to assist the penis in penetrating the vagina. It has its greatest usefulness in cases of psychological impotence. Pollock reports that a 30% watery solution of acetrizoate (Diaginol) is a good contrast medium with no complications in salpingography. Mann discusses spermicidal agents and classifies them into enzyme inhibitors, thiol reagents, and surface-active substances.

Farris's paper on timing of ovulation is most interesting. A hyperaemia test is used in which urine is injected subcutaneously and the ovary examined in two hours. Congestion increases daily. On the day of ovulation fading occurs—this means that ovulation will occur in six hours. In women with cycles of 23-31 days, conception took place on days 10-16 of the cycle. The majority occurred on day 12.

Parkes *et al.* discuss the biological and biochemical aspects of prevention of fertilization by enzyme inhibitors. Their conclusion is that compound 53D/K, which is related to Rehibin, inhibits hyaluronidase and other enzymes. Bishop discusses dilution effect on bull spermatozoa and shows that the O_2 uptake and motility is increased by dilution with normal saline. This is believed to be due to dilution of an inhibitor in the semen.

Palmer discusses gynaecological coelioscopy. This is an all-inclusive article pointing out history, indications,

dangers, and information gained by its use. The advantages of abdominal coelioscopy and vaginal coelioscopy in the knee-chest and dorsal position are discussed.

Russell compares the physique and medical history of a group of fertile and sub-fertile men. Malnutrition was not a factor in infertility. Urethritis was more common in the sub-fertile. Varicocele seemed to lower spermatogenesis. In half the cases no apparent reason for defective spermatogenesis could be found.

The articles are well-written, informative, authoritative, and have a good bibliography. This book should find a place in the library of anyone interested specifically in infertility.

The Royal College of Physicians and Surgeons of Canada

ANNOUNCEMENT OF EXAMINATIONS

Examinations are held for the Fellowship in Medicine and the Fellowship in Surgery, and for the Certificate in the approved medical and surgical specialties.

Applications for the 1956 Examinations will be received until April 30, 1956.

Regulations and Requirements of Graduate Training relating to the Examinations, as revised May 1951, application forms, lists of approved hospitals in Canada, and assessment of training application forms, may be obtained from:

The Honorary Secretary
The Royal College of Physicians and Surgeons of Canada
150 Metcalfe Street, Ottawa 4, Canada.



Children everywhere like it

infantol
The multi-vitamin for children

FRANK W. HORNER LIMITED

REFLECTIONS ON RENAL FUNCTION

J. R. Robinson, Assistant Director of Research, Department of Experimental Medicine, Medical Research Council and University of Cambridge, England. 163 pp. \$4.25. Charles C Thomas, Springfield, Illinois; The Ryerson Press, Toronto, 1954.

Reflections on Renal Function by James R. Robinson, M.D., Ph.D., of Cambridge University, is a most welcome addition to the literature in this field. The book is intended to fill the need for a somewhat advanced yet intermediate treatise. Its scope lies somewhere between that of the large detailed works devoted exclusively to this subject, and the more limited presentations found in physiology textbooks. Thus, the author explores our ignorance as well as our knowledge, and deals with hypotheses as well as facts. Within its 154 pages, this volume contains not only a succinct description of the salient features of renal physiology as they are now known, but also a thoughtful, stimulating and up-to-date analysis of the outstanding problems facing investigators in this field.

The author recognizes that a treatment of this type will inevitably reflect his own interpretations and viewpoints and will therefore be considered controversial by other renal physiologists. It would be easy to select a number of points of difference and quarrel with the author. For instance, the suggestion that tubular excretory processes play an insignificant role in the elaboration of the normal mammalian urine would be contested by many students of renal function. However, a resort to polemic would miss the main point of this book, which is not an incitement to argument, but an invitation to research. In this objective the author succeeds admirably.

The advanced student and investigator of renal function will find this a valuable and provocative monograph, a catalyst in the clarification of his own views and ideas, and a spur to further efforts to find the answers to the questions raised. The chapter which deals with the renal regulation of body fluid volume is especially valuable. The more recent pertinent observations are gathered together and organized into a well-integrated and logical analysis of the present status of this most important and perplexing problem. The readable and lucid style will provide any inquiring student of biology or practitioner of medicine with an entertaining and enlightening excursion into the borderlines of renal research, and furnish him with a broader basis for understanding the role which this organ plays in disease as well as in the normal economy of the organism.

ALCOHOLICS ANONYMOUS

The story of how many thousands of men and women have recovered from alcoholism. New and revised edition. 575 pp. \$4.50. Alcoholics Anonymous Publishing, Inc., New York, 1955.

The first edition of *Alcoholics Anonymous* was published in 1939. It was intended as a guidebook for those victims of alcoholic disease who had encountered the newly growing and vigorous fellowship of Alcoholics Anonymous. The book tells the story of Alcoholics Anonymous—how it was founded, what it stands for, how it works. This second edition was published in conjunction with the 20th anniversary of the organization. The new edition differs essentially from the first because of an increase in the number of personal biographies. There were 300,000 copies of the first edition sold, mostly to alcoholics, their families, their friends, and many others interested in their problems. It is estimated that 6,000 groups of Alcoholics Anonymous members exist throughout the world at the present time.

In addition to being a textbook for the A.A. member, *Alcoholics Anonymous* tells the story of the founders of this movement and of 36 typical persons who found a way to sobriety through this organization. The concept of the way to sobriety accepted by these people includes an intense spiritual approach but permits acceptance of God on any terms understandable to the person con-

cerned. The original model for the A.A. programme arose from an experience one man had in gaining his sobriety through the teachings of the Oxford Group prior to the founding of Alcoholics Anonymous in 1935.

This is not a medical or scientific book in any sense of the word, but these stories of the Alcoholics Anonymous members are impressive. Psychiatrists, psychologists, and other students of human problems will surely be forgiven if they encounter in these biographies some impression of the personality of these sick people and the particular ways in which an organization like Alcoholics Anonymous has worked for them.

It will be obvious that those who have obtained recovery through Alcoholics Anonymous are enthusiastic people. They are pleased at having accomplished what they thought would be impossible. We can understand, then, when they wish to carry the message of Alcoholics Anonymous to every problem drinker. It would appear, however, that the problem of recovery from this illness is more complex than this.

There are quotations in the book reporting on the endorsement of A.A. by various physicians who have found it helpful for their patients. Some of these endorsements are unbounded and unqualified and would suggest that here is a process which outstrips all the potential of modern medicine and the social sciences. It is difficult to believe that this is really the case.

It is unfortunate, but it must be said, that despite the phenomenal growth of Alcoholics Anonymous, despite the intense interest of professional people, and governmental and civic agencies, we have only begun to tackle the problem. Our alcoholic population is growing, and only a fraction of that population is obtaining help through any means whatsoever. The answer to this problem has not yet been found.

Alcoholics Anonymous tells the story of an astoundingly successful group method of dealing with some aspects of a human illness. It must not be ignored, but it must find its place in the wider picture of organized effort to tackle this major physical, mental and social problem.

SYMPOSIUM ON ATHEROSCLEROSIS

Held under the auspices of the Division of Medical Sciences, National Academy of Sciences, National Research Council, Washington, D.C. 249 pp. Illust. \$2.00. National Research Council Publication 338, National Academy of Sciences, Washington, D.C., 1954.

It is seldom that so much information up to date and pertinent to a problem can be found in one small book. The participants in this symposium have presented their work and views cogently and briefly. Almost without exception the short papers are of very high quality. The book will acquaint any interested reader with the most recent American experimental and research investigations into the problem of atherosclerosis. It is not recommended to the casual reader, but it is highly recommended to anyone with more than a passing interest in atherosclerosis and especially in the more recent trends in research on the problem.

PROCTOLOGIC ANATOMY

R. V. Gorsch, Clinical Professor of Proctology, New York Polyclinic Medical School and Hospital, New York. 310 pp. Illust. 2nd ed. \$8.00. The Williams and Wilkins Company, Baltimore; Burns & MacEachern, Toronto 2, 1955.

The appearance of a second edition of this monograph is justified by the contributions to our knowledge of pelvic anatomy made in the past 14 years. This volume makes available the detailed anatomy of the pelvic portion of the alimentary tract, the muscles of the pelvic outlet, and the pelvic fascia. It is written for the proctologist, but it will be read with interest and profit by all who are looking for help in the understanding of the anatomy of this difficult region.

